

## WEST Search History

DATE: Wednesday, June 06, 2007

Hide?	<u>Set</u> <u>Name</u>	<u>Query</u>	<u>Hit</u> <u>Count</u>
		<i>DB=PGPB,USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L1	((mitiglinide ) near12 (diabetic or diabetes or postprandial or glycemia or glucose or complication or hypoglycemia))	26

END OF SEARCH HISTORY

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	282	mitiglinide	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:15
S2	19	S1 AND @pd<"20030606"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/05/21 16:36
S3	282	mitiglinide or mitigilnide or mitglinide or mitiglnide or mitiginide	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/23 08:11
S4	24	S3 near11 (diabet\$ OR Diabetic OR diabetes or complication or glycemic or glucose)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/23 08:14
S5	275	S3 and (diabet\$ OR Diabetic OR diabetes or complication or glycemic or glucose)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/23 08:13
S6	184	S3 same (diabet\$ OR Diabetic OR diabetes or complication or glycemic or glucose)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/23 08:13
S7	142	S3 with (diabet\$ OR Diabetic OR diabetes or complication or glycemic or glucose)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 10:55

## EAST Search History

S8	285	mitiglinide or mitigilinide or mitglinide or mitiglnide or mitiginide	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 10:55
S9	143	S8 with (diabet\$ OR Diabetic OR diabetes or complication or glycemic or glucose)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 10:55
S10	143	S9	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 10:55
S11	751036	mitiglinide calcium hydrate	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 10:55
S13	28	mitiglinide calcium hydrate	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2007/05/24 10:56

## EAST Search History

S14	99	("20050267195" "20050215607" "6365176" "6251926" "20030040490" "20070072813" "6277877" "5981488" "6380223" "5932258" "20060188443" "4360019" "20050272640" "6268343" "6372244" "20050203001" "6376549" "6432993" "6143786" "6355635" "6287586" "6461870" "6458378" "6835400" "7183266" "20030012807" "20030017191" "20030125301" "20040185129" "5523087" "20060122244" "5597893" "6316429" "5919216" "20020193344" "20060257987" "20070037812" "20070066683" "20070082907" "6294538" "6362009" "6414149" "6414126" "6221633" "6221633" "6251905" "6297269" "6677358" "6316489" "6369075" ).pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:17
S15	98	("20050215607" "20050267195" "20030040490" "6251926" "6365176" "6268343" "6376549" "20060188443" "6432993" "20070072813" "5932258" "6380223" "6414126" "5981488" "6277877" "6380398" "6316038" "6323237" "6413946" "6440951" "6355635" "4360019" "6458378" "6835400" "7183266" "20030012807" "20030017191" "20030125301" "20040185129" "20050272640" "20040229774" "5284845" "6458924" "6258834" "6369075" "6399601" "6441015" "6451783" "20050143424" "6054587" "6287586" "6294672" "6461870" "5919216" "20060257987" "20070037812" "20070066683" "20070082907" "6329403" "6294538" ).pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:17
S16	128	S14 or S15	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:59

## EAST Search History

S17	285	mitiglinide	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:59
S18	121	S16 NOT S17	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:59
S19	569	(514/412).CCLS.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/05/25 11:25
S20	829	(514/310).CCLS.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/05/25 11:25
S21	1492	(514/563).CCLS.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/05/25 11:25
S22	2872	S19 or S20 or S21	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 11:26
S23	2243	S22 and @pd<"20050930"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 11:29

## EAST Search History

S24	1868	S22 and @pd<"20040930"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 11:29
S25	349	S19 and @pd<"20040930"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 11:30
S26	683	(S20 or S21) and diabetes	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 12:46
S27	794	(S20 or S21) and diabet\$	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 12:47
S28	399	S27 and @pd<"20040930"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 12:49
S29	792	S27 not S25	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 12:49
S30	792	S27 NOT S25	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 12:49

## EAST Search History

S31	1658	MIKOSHIBA.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:32
S32	309100	SUZUKI.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:32
S33	460206	SUZUKI, HISAO.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:32
S34	542	SUZUKI near HISAO.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:33
S36	26	KIYONO near YUJI.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:33
S38	2213	S31 or S34 or S36	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:34
S39	12	S38 and diabetes	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:34

## EAST Search History

S40	7	S38 and diabetes	USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/05/31 11:34
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ANSWER SUMMARY

L2 ANSWER 1 OF 1416 CAPLUS

Voltage regulator [machine translation]; 2007:536206 CAPLUS

L2 ANSWER 2 OF 1416 CAPLUS

An optical drive having a laser driver device with an adjustable power level; 2007:512519 CAPLUS

L2 ANSWER 3 OF 1416 CAPLUS

PCR detection of Reg IV mRNA for cancer diagnosis; 2007:485237 CAPLUS

L2 ANSWER 4 OF 1416 CAPLUS

2-Propenoic acid, methyl ester, polymer with ethenyl acetate, hydrolyzed, sodium salts; tolerance exemption; 2007:473041 CAPLUS

L2 ANSWER 5 OF 1416 CAPLUS

Roles of CD4+CD25+ T cells in the development of experimental murine allergic conjunctivitis; 2007:471425 CAPLUS

L1 ANSWER 1 OF 90 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L3 ANSWER 1 OF 4 REGISTRY

( $\alpha$ S,3aR,7aS)- octahydro- $\gamma$ -oxo- $\alpha$ -(phenylmethyl)-2H-Isoindole-2-butanoic acid, calcium salt (2:1); 145525-41-3 REGISTRY

L3 ANSWER 1 OF 4 REGISTRY

( $\alpha$ S,3aR,7aS)- octahydro- $\gamma$ -oxo- $\alpha$ -(phenylmethyl)-2H-Isoindole-2-butanoic acid, calcium salt (2:1); 145525-41-3 REGISTRY

L3 ANSWER 2 OF 4 REGISTRY

( $\alpha$ S,3aR,7aS)- octahydro- $\gamma$ -oxo- $\alpha$ -(phenylmethyl)-2H-Isoindole-2-butanoic acid; 145375-43-5 REGISTRY

L3 ANSWER 3 OF 4 REGISTRY

hydrochloride (1:2) 4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-Piperazineethanol; 146-56-5 REGISTRY

L3 ANSWER 4 OF 4 REGISTRY

4-chloro- $\alpha$ -(4-chlorophenyl)- $\alpha$ -(trichloromethyl)- Benzenemethanol; 115-32-2 REGISTRY

L7 ANSWER 1 OF 85 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L7 ANSWER 2 OF 85 CAPLUS

Carboxyl-glucuronidation of mitiglinide by human UDP-glucuronosyltransferases; 2007:453224 CAPLUS

L7 ANSWER 3 OF 85 CAPLUS

Mitiglinide and  $\alpha$ -glucosidase inhibitor combination for type 2 diabetes therapy; 2007:404898 CAPLUS

L7 ANSWER 4 OF 85 CAPLUS

Combination therapy for controlled carbohydrate digestion, decreased formation of intestinal gas, and modulation of insulin signaling or blood glucose levels; 2007:329618 CAPLUS

L7 ANSWER 5 OF 85 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287177 CAPLUS

L4 ANSWER 1 OF 6 CAPLUS

Characterization of the action of S 21403 (mitiglinide) on insulin secretion and biosynthesis in normal and diabetic  $\beta$ -cells; 2005:1205798 CAPLUS

L4 ANSWER 2 OF 6 CAPLUS

Pharmacological and clinical profile of mitiglinide calcium hydrate (Glufast), a new insulinotropic agent with rapid onset; 2004:836630 CAPLUS

L4 ANSWER 3 OF 6 CAPLUS

Rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride; 2004:496322 CAPLUS

L4 ANSWER 4 OF 6 CAPLUS

Rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial hyperglycemic agent: comparison with nateglinide; 2004:345396 CAPLUS

L4 ANSWER 5 OF 6 CAPLUS

Characterization of hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel hypoglycemic agent: comparison with glibenclamide, a sulfonylurea; 2004:345395 CAPLUS

L4 ANSWER 6 OF 6 CAPLUS

Effects of S 21403 on hormone secretion from isolated rat pancreas at different glucose concentrations; 2002:894053 CAPLUS

L1 ANSWER 1 OF 2 REGISTRY

( $\alpha$ S,3aR,7aS)- octahydro- $\gamma$ -oxo- $\alpha$ -(phenylmethyl)-2H-Isoindole-2-butanoic acid, calcium salt (2:1); 145525-41-3 REGISTRY

L3 ANSWER 1 OF 129 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L3 ANSWER 2 OF 129 CAPLUS

Mitiglinide and  $\alpha$ -glucosidase inhibitor combination for type 2 diabetes therapy; 2007:404898 CAPLUS

L3 ANSWER 3 OF 129 CAPLUS

Combination therapy for controlled carbohydrate digestion, decreased formation of intestinal gas, and modulation of insulin signaling or blood glucose levels; 2007:329618 CAPLUS

L3 ANSWER 4 OF 129 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287177 CAPLUS

L3 ANSWER 5 OF 129 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287142 CAPLUS

L3 ANSWER 6 OF 129 CAPLUS

Study on environmental risk assessment of drugs: excretion forms to environment; 2007:276713 CAPLUS

L3 ANSWER 7 OF 129 CAPLUS

High-performance liquid chromatography-electrospray ionization mass spectrometry determination of Mitiglinide in human plasma and its pharmacokinetics; 2007:207390 CAPLUS

L3 ANSWER 8 OF 129 CAPLUS

Sulfonylureas and glinides exhibit peroxisome proliferator-activated receptor  $\gamma$  activity: a combined virtual screening and biological assay approach; 2007:141807 CAPLUS

L3 ANSWER 9 OF 129 CAPLUS

Potassium channel blockers for treatment of migraine and headache; 2007:88262 CAPLUS

L3 ANSWER 10 OF 129 CAPLUS

Preparation of N-terminally modified GLP-1 receptor modulators and their use in the

treatment of diabetes and related conditions; 2006:1253322 CAPLUS

L5 ANSWER 1 OF 91 CAPLUS

Long-term effect of combination therapy with mitiglinide and once daily insulin glargine in patients who were successfully switched from intensive insulin therapy in short-term study; 2007:548465 CAPLUS

L5 ANSWER 2 OF 91 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L5 ANSWER 3 OF 91 CAPLUS

Carboxyl-glucuronidation of mitiglinide by human UDP-glucuronosyltransferases; 2007:453224 CAPLUS

L5 ANSWER 4 OF 91 CAPLUS

Mitiglinide and  $\alpha$ -glucosidase inhibitor combination for type 2 diabetes therapy; 2007:404898 CAPLUS

L5 ANSWER 5 OF 91 CAPLUS

Combination therapy for controlled carbohydrate digestion, decreased formation of intestinal gas, and modulation of insulin signaling or blood glucose levels; 2007:329618 CAPLUS

L5 ANSWER 6 OF 91 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287177 CAPLUS

L5 ANSWER 7 OF 91 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287142 CAPLUS

L5 ANSWER 8 OF 91 CAPLUS

Sulfonylureas and glinides exhibit peroxisome proliferator-activated receptor  $\gamma$  activity: a combined virtual screening and biological assay approach; 2007:141807 CAPLUS

L5 ANSWER 9 OF 91 CAPLUS

Preparation of N-terminally modified GLP-1 receptor modulators and their use in the treatment of diabetes and related conditions; 2006:1253322 CAPLUS

L5 ANSWER 10 OF 91 CAPLUS

Preparation of pyrazole compounds as hepatic glycogen phosphorylase inhibitors and therapeutic agents for diabetes; 2006:1252442 CAPLUS

L5 ANSWER 11 OF 91 CAPLUS

Combined pharmaceutical preparation for treatment of type 2 diabetes; 2006:1157536 CAPLUS

L5 ANSWER 12 OF 91 CAPLUS

Imaging docking and fusion of insulin granules induced by antidiabetes agents. Sulfonylurea and glinide drugs preferentially mediate the fusion of newcomer, but not previously docked, insulin granules; 2006:1056090 CAPLUS

L5 ANSWER 13 OF 91 CAPLUS

Process for preparation of isoindoline derivatives as antidiabetic agents; 2006:969655 CAPLUS

L5 ANSWER 14 OF 91 CAPLUS

Roflumilast for the treatment of diabetes mellitus; 2006:945768 CAPLUS

L5 ANSWER 15 OF 91 CAPLUS

Roflumilast for the treatment of diabetes mellitus and accompanying disorders, and combinations with other agents; 2006:944442 CAPLUS

L5 ANSWER 16 OF 91 CAPLUS

Effects of mitiglinide on glucose -induced insulin release into the portal vein and fat-induced triglyceride elevation in prediabetic and diabetic OLETF rats. [Erratum to document cited in CA145:262963]; 2006:898535 CAPLUS

L5 ANSWER 17 OF 91 CAPLUS

Manufacture and application of drug composition containing pioglitazone hydrochloride and mitiglinide for treating insulin-dependent diabetes mellitus; 2006:840773 CAPLUS

L5 ANSWER 18 OF 91 CAPLUS

Manufacture of dripping pill containing mitiglinide for treating diabetes mellitus; 2006:840772 CAPLUS

L5 ANSWER 19 OF 91 CAPLUS

Medicinal compositions containing hypoglycemic agents; 2006:766544 CAPLUS

L5 ANSWER 20 OF 91 CAPLUS

Manufacture of mitiglinide enteric-coated preparation; 2006:666684 CAPLUS

L5 ANSWER 21 OF 91 CAPLUS

Effects of mitiglinide on glucose -induced insulin release into the portal vein and fat-induced triglyceride elevation in prediabetic and diabetic OLETF rats; 2006:664881 CAPLUS

L5 ANSWER 22 OF 91 CAPLUS

Mitiglinide sustained-release preparation and its production method; 2006:519723 CAPLUS

L5 ANSWER 23 OF 91 CAPLUS

Therapeutic efficacy of mitiglinide combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine in patients with type 2 diabetes mellitus; 2006:505268 CAPLUS

L5 ANSWER 24 OF 91 CAPLUS

Synthesis and hypoglycemic activity of mitiglinide analogs; 2006:328612 CAPLUS

L5 ANSWER 25 OF 91 CAPLUS

Mitiglinide oral preparations for the treatment of diabetes; 2006:220560 CAPLUS

L5 ANSWER 26 OF 91 CAPLUS

Rapid insulin secretagogue: Mitiglinide; 2006:64372 CAPLUS

L5 ANSWER 27 OF 91 CAPLUS

Manufacture of compound hypoglycemic drug containing mitiglinide and metformin hydrochloride; 2006:39395 CAPLUS

L5 ANSWER 28 OF 91 CAPLUS

Pharmaceutical composition for prevention or treatment of lipid metabolism disorder; 2005:1220708 CAPLUS

L5 ANSWER 29 OF 91 CAPLUS

Characterization of the action of S 21403 ( mitiglinide) on insulin secretion and biosynthesis in normal and diabetic  $\beta$ -cells; 2005:1205798 CAPLUS

L5 ANSWER 30 OF 91 CAPLUS

Effects of S21403 (mitiglinide) on postprandial generation of oxidative stress and inflammation in type 2 diabetic patients; 2005:1009580 CAPLUS

L5 ANSWER 31 OF 91 CAPLUS

Method for examining blood glucose control state; 2005:962511 CAPLUS

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Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases; 2005:120729 CAPLUS

L5 ANSWER 33 OF 91 CAPLUS

Rapid acting insulin secretagogue in treatment for type 2 diabetes; 2005:43407 CAPLUS

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The impact of ATP-sensitive K<sup>+</sup> channel subtype selectivity of insulin secretagogues for the coronary vasculature and the myocardium; 2004:1076146 CAPLUS

L5 ANSWER 35 OF 91 CAPLUS

Mitiglinide calcium dihydrate; 2004:1072015 CAPLUS

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Synthesis of antidiabetic mitiglinide calcium hydrate; 2004:1070406 CAPLUS

L5 ANSWER 37 OF 91 CAPLUS

A synergistic pharmaceutical combination comprising cicletanine for the prevention or treatment of diabetes; 2004:902180 CAPLUS

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Pharmacological and clinical profile of mitiglinide calcium hydrate (Glufast), a new insulintropic agent with rapid onset; 2004:836630 CAPLUS

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Remedy for diabetes; 2004:681582 CAPLUS

L5 ANSWER 40 OF 91 CAPLUS

Rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride; 2004:496322 CAPLUS

L5 ANSWER 41 OF 91 CAPLUS

Rapid onset-insulintropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial hyperglycemic agent: comparison with nateglinide; 2004:345396 CAPLUS

L5 ANSWER 42 OF 91 CAPLUS

Characterization of hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel hypoglycemic agent: comparison with glibenclamide, a sulfonylurea; 2004:345395 CAPLUS

L5 ANSWER 43 OF 91 CAPLUS

Preparation of aroylhydroxypyrazoles for treatment of metabolic disorders; 2004:333698 CAPLUS

L5 ANSWER 44 OF 91 CAPLUS

Cardiovascular risk in type 2 diabetics and pharmacological regulation of mealtime glucose excursions; 2004:202949 CAPLUS

L5 ANSWER 45 OF 91 CAPLUS

Bicyclic oligopeptides and their use as glucagon receptor antagonists; 2004:60541 CAPLUS

L5 ANSWER 46 OF 91 CAPLUS

Bicyclic oligopeptides and their use as glucagon receptor antagonists; 2004:60532 CAPLUS

L5 ANSWER 47 OF 91 CAPLUS

Drug composition for prevention or inhibition of advance of diabetic complication; 2004:20487 CAPLUS

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Drug composition for blood sugar control; 2004:20486 CAPLUS

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Antidiabetic preparation for oral administration; 2004:3671 CAPLUS

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Pharmacology of the meglitinide analogs: new treatment options for type 2 diabetes mellitus; 2003:1000347 CAPLUS

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Therapeutic agent for diabetes; 2003:931184 CAPLUS

L5 ANSWER 52 OF 91 CAPLUS

Uptake of tritiated mitiglinide by pancreatic pieces and islets; 2003:780556 CAPLUS

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Combination of a HMG-CoA reductase inhibitor and an insulin secretion enhancer; 2003:777602 CAPLUS

L5 ANSWER 54 OF 91 CAPLUS

Oral pharmaceutical composition containing mitiglinide; 2003:573217 CAPLUS

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Use of an immediate-release powder in pharmaceutical and nutraceutical compositions; 2003:511859 CAPLUS

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Pharmaceutical compositions containing a renin inhibitor and antidiabetics; 2003:473243 CAPLUS

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Synergistic antidiabetic combinations containing antihyperlipemics and hydroximic acids; 2003:76614 CAPLUS

L5 ANSWER 58 OF 91 CAPLUS

Effects of S 21403 on hormone secretion from isolated rat pancreas at different glucose concentrations; 2002:894053 CAPLUS

L5 ANSWER 59 OF 91 CAPLUS

Processes for preparation of optically active 2-benzylsuccinic acid and optically active 2-benzylsuccinic acid monoamides; 2002:832745 CAPLUS

L5 ANSWER 60 OF 91 CAPLUS

Study of the insulinotropic effect of the novel antihyperglycemic agent KAD-1229 using HIT T15 cells, a hamster's insulinoma cell line; 2002:743481 CAPLUS

L5 ANSWER 61 OF 91 CAPLUS

Compositions comprising a polypeptide and an active agent; 2002:556104 CAPLUS

L5 ANSWER 62 OF 91 CAPLUS

Effect of KAD-1229, a novel hypoglycaemic agent, on plasma glucose levels after meal load in type 2 diabetic rats; 2002:395747 CAPLUS

L5 ANSWER 63 OF 91 CAPLUS

Compositions comprising a polypeptide and an active agent; 2002:332011 CAPLUS

L5 ANSWER 64 OF 91 CAPLUS

Drugs for diabetes, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester; 2002:293592 CAPLUS

L5 ANSWER 65 OF 91 CAPLUS

Pharmaceutical compositions containing AT-receptor antagonist or insulin secretion enhancers; 2002:157602 CAPLUS

L5 ANSWER 66 OF 91 CAPLUS

Combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors; 2002:157564 CAPLUS

L5 ANSWER 67 OF 91 CAPLUS

A combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for the treatment of diabetes; 2002:51257 CAPLUS

L5 ANSWER 68 OF 91 CAPLUS

Absence of exacerbation of myocardial stunning in anesthetized dogs treated with KAD-1229, a novel hypoglycemic agent; 2001:864540 CAPLUS

L5 ANSWER 69 OF 91 CAPLUS

The effects of mitiglinide (KAD-1229), a new antidiabetic drug, on ATP-sensitive K<sup>+</sup> channels and insulin secretion: comparison with the sulfonylureas and nateglinide; 2001:857058 CAPLUS

L5 ANSWER 70 OF 91 CAPLUS

Antidiabetic agents containing  $\alpha$ -glucosidase inhibitors and insulin secretion promoters; 2001:635931 CAPLUS

L5 ANSWER 71 OF 91 CAPLUS

Rapid acting insulintropic agents: restoration of early insulin secretion as a physiologic approach to improve glucose control; 2001:620286 CAPLUS

L5 ANSWER 72 OF 91 CAPLUS

Effects of mitiglinide (s 21403) on Kir6.2/SUR1, Kir6.2/SUR2A and Kir6.2/SUR2B types of ATP-sensitive potassium channel; 2001:282226 CAPLUS

L5 ANSWER 73 OF 91 CAPLUS

Effect of KAD-1229, a nonsulfonylurea hypoglycemic agent, on plasma glucose and insulin in streptozotocin-induced diabetic dogs; 2001:166771 CAPLUS

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Immediate-release oral pharmaceutical compositions containing benzylsuccinate derivatives; 2000:841976 CAPLUS

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Use of succinic acid derivatives to obtain a medicine for treating inflammation; 2000:814308 CAPLUS

L5 ANSWER 76 OF 91 CAPLUS

Recent developments and emerging therapies for type 2 diabetes mellitus; 2000:194936 CAPLUS

L5 ANSWER 77 OF 91 CAPLUS

Antidiabetic oral formulations containing benzylsuccinic acid derivative; 2000:59962 CAPLUS

L5 ANSWER 78 OF 91 CAPLUS

Effect of the Meglitinide analog S21403 on cationic fluxes and insulin release in perfused rat pancreatic islets exposed to a high concentration of D- Glucose; 1999:573477 CAPLUS

L5 ANSWER 79 OF 91 CAPLUS

Process for producing benzylsuccinic acid derivatives; 1998:527315 CAPLUS

L5 ANSWER 80 OF 91 CAPLUS

Process for producing optically active benzylsuccinic acid by optical resolution; 1998:527305 CAPLUS

L5 ANSWER 81 OF 91 CAPLUS

Effect of a novel hypoglycemic agent, KAD-1229 on glucose metabolism and fructose-2, 6- biphosphate content in isolated hepatocytes of normal rats; 1996:730982 CAPLUS

L5 ANSWER 82 OF 91 CAPLUS

Effect of the meglitinide analog KAD-1229 on <sup>45</sup>Ca outflow and insulin release in

pancreatic islets; 1996:647356 CAPLUS

L5 ANSWER 83 OF 91 CAPLUS

Effects of the methyl esters of pyruvate, succinate and glutamate on the secretory response to meglitinide analogs in rat pancreatic islets; 1996:584776 CAPLUS

L5 ANSWER 84 OF 91 CAPLUS

A rapid- and short-acting hypoglycemic agent KAD-1229 improves post-prandial hyperglycemia and diabetic complications in streptozotocin-induced non-insulin-dependent diabetes mellitus rats; 1996:536607 CAPLUS

L5 ANSWER 85 OF 91 CAPLUS

Effect of a non-sulfonylurea hypoglycemic agent, KAD-1229 on hormone secretion in the isolated perfused pancreas of the rat; 1996:269911 CAPLUS

L5 ANSWER 86 OF 91 CAPLUS

Insulinotropic action of meglitinide analogs: modulation by an activator of ATP-sensitive K<sup>+</sup> channels and high extracellular K<sup>+</sup> concentrations; 1996:156362 CAPLUS

L5 ANSWER 87 OF 91 CAPLUS

Insulinotropic action of (2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)propionate I. Secretory and cationic aspects; 1995:747679 CAPLUS

L5 ANSWER 88 OF 91 CAPLUS

Normalization of impaired glucose tolerance by the short-acting hypoglycemic agent calcium (2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)propionate dihydrate (KAD-1229) in non-insulin-dependent diabetes mellitus rats; 1995:477544 CAPLUS

L5 ANSWER 89 OF 91 CAPLUS

Inhibition of ATP-sensitive K<sup>+</sup> channel by a non-sulfonylurea compound KAD-1229 in a pancreatic  $\beta$ -cell line, MIN 6 cell; 1995:231935 CAPLUS

L5 ANSWER 90 OF 91 CAPLUS

Novel rapid- and short-acting hypoglycemic agent, a calcium(2s)- 2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)propionate (KAD-1229) that acts on the sulfonylurea receptor: comparison of effects between KAD-1229 and gliclazide; 1994:426648 CAPLUS

L5 ANSWER 91 OF 91 CAPLUS

Preparation of succinic acid azabicycliclamides and related compounds as antidiabetics; 1993:59584 CAPLUS



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Welcome to STN International! Enter x:x

LOGINID:ssptamrf1614

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

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NEWS	3	JAN 16	CA/CAPLUS Company Name Thesaurus enhanced and reloaded
NEWS	4	JAN 16	IPC version 2007.01 thesaurus available on STN
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NEWS	6	JAN 22	CA/CAPLUS updated with revised CAS roles
NEWS	7	JAN 22	CA/CAPLUS enhanced with patent applications from India
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NEWS	31	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS	32	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS	33	MAY 21	CA/CAPLUS enhanced with additional kind codes for German patents
NEWS	34	MAY 22	CA/CAPLUS enhanced with IPC reclassification in Japanese patents
NEWS EXPRESS		NOVEMBER 10	CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
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Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 17:36:28 ON 22 MAY 2007

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 17:36:43 ON 22 MAY 2007

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=> e mitiglinide

E1	1	MITIGEAGE/BI
E2	1	MITIGEN/BI
E3	90 -->	MITIGLINIDE/BI
E4	1	MITIGLNIDE/BI
E5	4	MITIGRATION/BI
E6	1	MITIGATION/BI
E7	2	MITII/BI
E8	1	MITIKAS/BI
E9	1	MITIKO/BI
E10	1	MITIKOGANE/BI
E11	1	MITILAN/BI
E12	3	MITILANE/BI

=> s e3-4

90 MITIGLINIDE/BI  
1 MITIGLNIDE/BI

L1 90 (MITIGLINIDE/BI OR MITIGLNIDE/BI)

=> s reg

1347 REG

82 REGS

L2 1416 REG

(REG OR REGS)

=> d l2 1-5 ibib

.L2 ANSWER 1 OF 1416 CAPLUS COPYRIGHT 2007 ACS on STN

.L2 ANSWER 2 OF 1416 CAPLUS COPYRIGHT 2007 ACS on STN

.L2 ANSWER 3 OF 1416 CAPLUS COPYRIGHT 2007 ACS on STN

.L2 ANSWER 4 OF 1416 CAPLUS COPYRIGHT 2007 ACS on STN

.L2 ANSWER 5 OF 1416 CAPLUS COPYRIGHT 2007 ACS on STN

=> his

HIS IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> d his

(FILE 'HOME' ENTERED AT 17:36:28 ON 22 MAY 2007)

FILE 'CAPLUS' ENTERED AT 17:36:43 ON 22 MAY 2007

E MITIGLINIDE

L1 90 S E3-4

L2 1416 S REG

=> s l1 AND diabet

=> d l1 IBIB

.L1 ANSWER 1 OF 90 CAPLUS COPYRIGHT 2007 ACS on STN

=> file registry

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

16.87

17.08

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Property values tagged with IC are from the ZIC/VINITI data file  
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STRUCTURE FILE UPDATES: 21 MAY 2007 HIGHEST RN 935505-97-8

DICTIONARY FILE UPDATES: 21 MAY 2007 HIGHEST RN 935505-97-8

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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=> e mitiglinide

E1	1	MITIGAL/BI
E2	1	MITIGAN/BI
E3	2 -->	MITIGLINIDE/BI
E4	1	MITIL/BI
E5	14	MITILYSIN/BI
E6	10	MITIN/BI
E7	1	MITINDO/BI
E8	1	MITINDOMIDE/BI
E9	4	MITINE/BI
E10	2	MITION/BI
E11	3	MITIPH/BI
E12	3	MITIPHYL/BI

=> s e2-e4

	1	MITIGAN/BI
	2	MITIGLINIDE/BI
	1	MITIL/BI
L3	4	(MITIGAN/BI OR MITIGLINIDE/BI OR MITIL/BI)

=> d

.L3 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

=> d l3 1-4

.L3 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

.L3 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

.L3 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

.L3 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

27.30

44.38

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=> s 145525-41-3 OR mitiglinide  
REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...  
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L5 53 L4

L6 90 MITIGLINIDE  
128 L5 OR MITIGLINIDE

=> s l6 and (diabetes OR diabetic OR diabetic complication OR postprandial hypoglycemia OR glycemic control or glucose)

125073 DIABETES  
65399 DIABETIC  
9086 DIABETICS  
69423 DIABETIC  
(DIABETIC OR DIABETICS)  
65399 DIABETIC  
9086 DIABETICS  
69423 DIABETIC  
(DIABETIC OR DIABETICS)  
12197 COMPLICATION  
35072 COMPLICATIONS  
44255 COMPLICATION  
(COMPLICATION OR COMPLICATIONS)  
2688 DIABETIC COMPLICATION  
(DIABETIC(W)COMPLICATION)  
7857 POSTPRANDIAL  
1 POSTPRANDIALS  
7857 POSTPRANDIAL  
(POSTPRANDIAL OR POSTPRANDIALS)  
13989 HYPOGLYCEMIA  
48 HYPOGLYCEMIAS  
14010 HYPOGLYCEMIA  
(HYPOGLYCEMIA OR HYPOGLYCEMIAS)  
37 POSTPRANDIAL HYPOGLYCEMIA  
(POSTPRANDIAL(W)HYPOGLYCEMIA)  
6108 GLYCEMIC  
1587652 CONTROL  
336796 CONTROLS

1806258 CONTROL  
(CONTROL OR CONTROLS)  
3436 GLYCEMIC CONTROL  
(GLYCEMIC(W)CONTROL)

423129 GLUCOSE  
823 GLUCOSES

423309 GLUCOSE  
(GLUCOSE OR GLUCOSES)

L7 85 L6 AND (DIABETES OR DIABETIC OR DIABETIC COMPLICATION OR POSTPRA  
NDIAL HYPOGLYCEMIA OR GLYCEMIC CONTROL OR GLUCOSE)

=> d 1-5 ibib

.L7 ANSWER 1 OF 85 CAPLUS COPYRIGHT 2007 ACS on STN

.L7 ANSWER 2 OF 85 CAPLUS COPYRIGHT 2007 ACS on STN

.L7 ANSWER 3 OF 85 CAPLUS COPYRIGHT 2007 ACS on STN

.L7 ANSWER 4 OF 85 CAPLUS COPYRIGHT 2007 ACS on STN

.L7 ANSWER 5 OF 85 CAPLUS COPYRIGHT 2007 ACS on STN

=> FIL STNGUIDE

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

29.89

75.19

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=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.06

75.25

STN INTERNATIONAL LOGOFF AT 17:48:21 ON 22 MAY 2007

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LOGINID:ssptamrf1614

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field  
NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE  
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NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases  
  
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NEWS 30 MAY 14 RDISCLOSURE on STN Easy enhanced with new search and display fields  
  
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FILE 'HOME' ENTERED AT 17:50:50 ON 22 MAY 2007

=> d his

(FILE 'HOME' ENTERED AT 17:50:50 ON 22 MAY 2007)

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'CAPLUS' ENTERED AT 17:51:10 ON 22 MAY 2007

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=> d his

(FILE 'HOME' ENTERED AT 17:50:50 ON 22 MAY 2007)

FILE 'CAPLUS' ENTERED AT 17:51:10 ON 22 MAY 2007

=> s 145525-41-3

REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L2

53 L1

=> s 12 and mitiglinide

90 MITIGLINIDE



L3 15 L2 AND MITIGLINIDE

=> s l3 and (diabetic or diabetes or diabetic complication or postprandial or glycemie or glucose)

65399 DIABETIC  
9086 DIABETICS  
69423 DIABETIC  
(DIABETIC OR DIABETICS)  
125073 DIABETES  
65399 DIABETIC  
9086 DIABETICS  
69423 DIABETIC  
(DIABETIC OR DIABETICS)  
12197 COMPLICATION  
35072 COMPLICATIONS  
44255 COMPLICATION  
(COMPLICATION OR COMPLICATIONS)  
2688 DIABETIC COMPLICATION  
(DIABETIC(W)COMPLICATION)  
7857 POSTPRANDIAL  
1 POSTPRANDIALS  
7857 POSTPRANDIAL  
(POSTPRANDIAL OR POSTPRANDIALS)  
6108 GLYCEMIC  
423129 GLUCOSE  
823 GLUCOSES  
423309 GLUCOSE  
(GLUCOSE OR GLUCOSES)

L4 6 L3 AND (DIABETIC OR DIABETES OR DIABETIC COMPLICATION OR POSTPRANDIAL OR GLYCEMIC OR GLUCOSE)

=> d 1-6

.L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

.L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

.L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

.L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

.L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

.L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

=> FIL STNGUIDE

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

26.11

27.24

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: May 18, 2007 (20070518/UP).

```
=> save
ENTER L#, L# RANGE, ALL, OR (END):all
ENTER NAME OR (END):10519102
10519102 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query,
answer set, or L-number list. The name must:
  1. Begin with a letter,
  2. Have 1-12 characters,
  3. Contain only letters (A-Z) and numbers (0-9),
  4. End with /Q for a query (search profile,
    structure, or screen set), /A for an answer
    set, or /L for an L-number list.
  5. Not already be in use as a saved name,
  6. Not be END, SAV, SAVE, SAVED
  7. Not have the form of an L-number (Lnnn).
ENTER NAME OR (END):finn10519102
FINN10519102 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query,
answer set, or L-number list. The name must:
  1. Begin with a letter,
  2. Have 1-12 characters,
  3. Contain only letters (A-Z) and numbers (0-9),
  4. End with /Q for a query (search profile,
    structure, or screen set), /A for an answer
    set, or /L for an L-number list.
  5. Not already be in use as a saved name,
  6. Not be END, SAV, SAVE, SAVED
  7. Not have the form of an L-number (Lnnn).
ENTER NAME OR (END):finn519102
FINN519102 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query,
answer set, or L-number list. The name must:
  1. Begin with a letter,
  2. Have 1-12 characters,
  3. Contain only letters (A-Z) and numbers (0-9),
  4. End with /Q for a query (search profile,
    structure, or screen set), /A for an answer
    set, or /L for an L-number list.
  5. Not already be in use as a saved name,
  6. Not be END, SAV, SAVE, SAVED
  7. Not have the form of an L-number (Lnnn).
ENTER NAME OR (END):finn519102/a
'FINN519102/A' IS NOT ALLOWED WITH ALL
The saved name of an L# list must end with '/L'.

=> SAVE L1,L2,L3,L4 FINN10519102/L
L# LIST L1,L2,L3,L4 HAS BEEN SAVED AS 'FINN10519102/L'

=> log off
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
STN INTERNATIONAL LOGOFF AT 17:55:43 ON 22 MAY 2007
```

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamrf1614

PASSWORD:  
TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

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NEWS 32 MAY 21 TOXCENTER enhanced with BIOSIS reload  
NEWS 33 MAY 21 CA/CAPLUS enhanced with additional kind codes for German patents  
NEWS 34 MAY 22 CA/CAPLUS enhanced with IPC reclassification in Japanese patents  
  
NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.  
  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS LOGIN Welcome Banner and News Items  
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 14:30:38 ON 30 MAY 2007

=> file registry

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 14:31:12 ON 30 MAY 2007

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 MAY 2007 HIGHEST RN 936074-26-9

DICTIONARY FILE UPDATES: 29 MAY 2007 HIGHEST RN 936074-26-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

=> s mitiglinide

L1 2 MITIGLINIDE

=> d l1

.L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2007 ACS on STN

=> s l1

L2 2 MITIGLINIDE

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

13.20

13.41

FILE 'CAPLUS' ENTERED AT 14:33:11 ON 30 MAY 2007

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE COVERS 1907 - 30 May 2007 VOL 146 ISS 23  
FILE LAST UPDATED: 29 May 2007 (20070529/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s l1

L3 129 L1

=> d l3 1-10 IBIB

.L3 ANSWER 1 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 2 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 3 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 4 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 5 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 6 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 7 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 8 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 9 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 10 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

=> d his

(FILE 'HOME' ENTERED AT 14:30:38 ON 30 MAY 2007)

FILE 'REGISTRY' ENTERED AT 14:31:12 ON 30 MAY 2007

L1 2 S MITIGLINIDE

L2 2 S L1

FILE 'CAPLUS' ENTERED AT 14:33:11 ON 30 MAY 2007

L3 129 S L1

=> e mitiglinide

E1 1 MITIGEAGE/BI

E2 1 MITIGEN/BI

E3 91 --> MITIGLINIDE/BI

E4 1 MITIGLNIDE/BI

E5	4	MITIGATION/BI
E6	1	MITIGATION/BI
E7	2	MITII/BI
E8	1	MITIKAS/BI
E9	1	MITIKO/BI
E10	1	MITIKOGANE/BI
E11	1	MITILAN/BI
E12	3	MITILANE/BI

=> s L3 or mitiglinide

	91	MITIGLINIDE
L4	139	L3 OR MITIGLINIDE

=> s 4 and (diabetes or diabet or postprandial or diatbetic or glycemc or complication or (glucose level))

OR IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

For a list of commands available to you in the current file, enter

"HELP COMMANDS" at an arrow prompt (=>).

=> s l4 and (diabetes or diabet or postprandial or diabetic or glycemc or complication or (glucose level))

OR IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

For a list of commands available to you in the current file, enter

"HELP COMMANDS" at an arrow prompt (=>).

=> s l4 and (diabetic or diabetes or postprandial or glycemc or complication or glucose)

	65527	DIABETIC
	9096	DIABETICS
	69552	DIABETIC
		(DIABETIC OR DIABETICS)
125400		DIABETES
	7888	POSTPRANDIAL
	1	POSTPRANDIALS
	7888	POSTPRANDIAL
		(POSTPRANDIAL OR POSTPRANDIALS)
	6137	GLYCEMIC
12238		COMPLICATION
35176		COMPLICATIONS
44391		COMPLICATION
		(COMPLICATION OR COMPLICATIONS)
423650		GLUCOSE
	823	GLUCOSES
423830		GLUCOSE
		(GLUCOSE OR GLUCOSES)

L5	91	L4 AND (DIABETIC OR DIABETES OR POSTPRANDIAL OR GLYCEMIC OR COMPLICATION OR GLUCOSE)
----	----	--

=> save

ENTER L#, L# RANGE, ALL, OR (END):all

ENTER NAME OR (END):10519155

10519155 IS NOT A VALID SAVED NAME

Enter the name you wish to use for the saved query, answer set, or L-number list. The name must:

1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile, structure, or screen set), /A for an answer set, or /L for an L-number list.
5. Not already be in use as a saved name,

6. Not be END, SAV, SAVE, SAVED  
7. Not have the form of an L-number (Lnnn).  
ENTER NAME OR (END):finn053007  
FINN053007 IS NOT A VALID SAVED NAME  
Enter the name you wish to use for the saved query,  
answer set, or L-number list. The name must:

1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile,  
structure, or screen set), /A for an answer  
set, or /L for an L-number list.
5. Not already be in use as a saved name,
6. Not be END, SAV, SAVE, SAVED
7. Not have the form of an L-number (Lnnn).

ENTER NAME OR (END):finn5307  
FINN5307 IS NOT A VALID SAVED NAME  
Enter the name you wish to use for the saved query,  
answer set, or L-number list. The name must:

1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile,  
structure, or screen set), /A for an answer  
set, or /L for an L-number list.
5. Not already be in use as a saved name,
6. Not be END, SAV, SAVE, SAVED
7. Not have the form of an L-number (Lnnn).

ENTER NAME OR (END):finn530  
FINN530 IS NOT A VALID SAVED NAME  
Enter the name you wish to use for the saved query,  
answer set, or L-number list. The name must:

1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile,  
structure, or screen set), /A for an answer  
set, or /L for an L-number list.
5. Not already be in use as a saved name,
6. Not be END, SAV, SAVE, SAVED
7. Not have the form of an L-number (Lnnn).

ENTER NAME OR (END):finn5  
FINN5 IS NOT A VALID SAVED NAME  
Enter the name you wish to use for the saved query,  
answer set, or L-number list. The name must:

1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile,  
structure, or screen set), /A for an answer  
set, or /L for an L-number list.
5. Not already be in use as a saved name,
6. Not be END, SAV, SAVE, SAVED
7. Not have the form of an L-number (Lnnn).

ENTER NAME OR (END):finn053007/a  
'FINN053007/A' IS NOT ALLOWED WITH ALL  
The saved name of an L# list must end with '/L'.

=> finn053007/1  
FINN053007 IS NOT A RECOGNIZED COMMAND  
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> FIL STNGUIDE  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
31.98	45.39

FULL ESTIMATED COST

FILE 'STNGUIDE' ENTERED AT 14:40:55 ON 30 MAY 2007  
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT  
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FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: May 25, 2007 (20070525/UP).

=> SAVE L1,L2,L3,L4,L5 FINN053007/L  
L# LIST L1,L2,L3,L4,L5 HAS BEEN SAVED AS 'FINN053007/L'

=> log hold  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.06	45.45

FULL ESTIMATED COST

SESSION WILL BE HELD FOR 120 MINUTES  
STN INTERNATIONAL SESSION SUSPENDED AT 14:41:35 ON 30 MAY 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamrf1614

PASSWORD:

\* \* \* \* \* RECONNECTED TO STN INTERNATIONAL \* \* \* \* \*  
SESSION RESUMED IN FILE 'STNGUIDE' AT 14:46:39 ON 30 MAY 2007  
FILE 'STNGUIDE' ENTERED AT 14:46:39 ON 30 MAY 2007  
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.06	45.45

FULL ESTIMATED COST

=> dis his

(FILE 'HOME' ENTERED AT 14:30:38 ON 30 MAY 2007)

FILE 'REGISTRY' ENTERED AT 14:31:12 ON 30 MAY 2007

L1 2 S MITIGLINIDE  
L2 2 S L1

FILE 'CAPLUS' ENTERED AT 14:33:11 ON 30 MAY 2007

L3 129 S L1  
E MITIGLINIDE

L4 139 S L3 OR MITIGLINIDE

L5 91 S L4 AND (DIABETIC OR DIABETES OR POSTPRANDIAL OR GLYCEMIC OR C

FILE 'STNGUIDE' ENTERED AT 14:40:55 ON 30 MAY 2007  
SAVE L1,L2,L3,L4,L5 FINN053007/L

=> s l5 and diabetes  
0 MITIGLINIDE



0 MITIGLINIDE  
0 DIABETIC  
1 DIABETES  
0 POSTPRANDIAL  
0 GLYCEMIC  
0 COMPLICATION  
0 GLUCOSE  
1 DIABETES  
0 L5 AND DIABETES

L6

=> d l5 1-91 ibib

YOU HAVE REQUESTED DATA FROM FILE 'CAPLUS' - CONTINUE? (Y)/N:y

- .L5 ANSWER 1 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 2 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 3 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 4 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 5 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 6 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 7 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 8 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 9 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 10 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 11 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 12 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
- .L5 ANSWER 13 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
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- .L5 ANSWER 15 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
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- 。L5 ANSWER 24 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN
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.L5 ANSWER 89 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN  
.L5 ANSWER 90 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN  
.L5 ANSWER 91 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

=> log hold

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.06	153.54

FULL ESTIMATED COST

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 14:48:59 ON 30 MAY 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamrf1614

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1	Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 08 CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	3	JAN 16 CA/Caplus Company Name Thesaurus enhanced and reloaded

NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN  
 NEWS 5 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data  
 NEWS 6 JAN 22 CA/CAPLUS updated with revised CAS roles  
 NEWS 7 JAN 22 CA/CAPLUS enhanced with patent applications from India  
 NEWS 8 JAN 29 PHAR reloaded with new search and display fields  
 NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in multiple databases  
 NEWS 10 FEB 15 PATDPASPC enhanced with Drug Approval numbers  
 NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records  
 NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality  
 NEWS 13 FEB 26 MEDLINE reloaded with enhancements  
 NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field  
 NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE  
 NEWS 16 FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements  
 NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases  
 NEWS 18 MAR 15 WPIDS/WPIX enhanced with new FRAGHITSTR display format  
 NEWS 19 MAR 16 CASREACT coverage extended  
 NEWS 20 MAR 20 MARPAT now updated daily  
 NEWS 21 MAR 22 LWPI reloaded  
 NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements  
 NEWS 23 APR 02 JICST-EPLUS removed from database clusters and STN  
 NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field  
 NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records  
 NEWS 26 APR 30 CA/CAPLUS enhanced with 1870-1889 U.S. patent records  
 NEWS 27 APR 30 INPADOC replaced by INPADOCDB on STN  
 NEWS 28 MAY 01 New CAS web site launched  
 NEWS 29 MAY 08 CA/CAPLUS Indian patent publication number format defined  
 NEWS 30 MAY 14 RDISCLOSURE on STN Easy enhanced with new search and display fields  
 NEWS 31 MAY 21 BIOSIS reloaded and enhanced with archival data  
 NEWS 32 MAY 21 TOXCENTER enhanced with BIOSIS reload  
 NEWS 33 MAY 21 CA/CAPLUS enhanced with additional kind codes for German patents  
 NEWS 34 MAY 22 CA/CAPLUS enhanced with IPC reclassification in Japanese patents  
  
 NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.  
  
 NEWS HOURS STN Operating Hours Plus Help Desk Availability  
 NEWS LOGIN Welcome Banner and News Items  
 NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 17:53:06 ON 06 JUN 2007

=> activate

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of

commands which can be used in this file.

=> activate saved

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> d his

(FILE 'HOME' ENTERED AT 17:53:06 ON 06 JUN 2007)

=> saved

SAVED IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> activate 102/A

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> log off

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:y

STN INTERNATIONAL LOGOFF AT 17:54:19 ON 06 JUN 2007

10/519155

\*\*\*\*\* QUERY RESULTS \*\*\*\*\*

=> d his 133

(FILE 'HCAPLUS' ENTERED AT 14:40:20 ON 24 MAY 2007)

L33 24 S L32 OR L24

=> d que 133

L4 1 SEA FILE=REGISTRY ABB=ON PLU=ON 145375-43-5/RN  
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON 207844-01-7/RN  
L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON MITIGLINIDE/CN  
L8 2 SEA FILE=REGISTRY ABB=ON PLU=ON (L4 OR L5 OR L6)  
L9 97 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR MITIGLINIDE CALCIUM  
HYDRATE/OBI  
L10 87 SEA FILE=HCAPLUS ABB=ON PLU=ON MITIGLINIDE/OBI OR MITI/OBI(W)  
GLINIDE/OBI  
L11 108 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 OR L10  
L13 2160940 SEA FILE=HCAPLUS ABB=ON PLU=ON (INHIBIT?/OBI OR HINDER?/OBI  
OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR  
PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI)  
L19 110617 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABET?/OBI  
L20 54 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND L19  
L22 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 (5A) L20  
L23 QUE ABB=ON PLU=ON AY<2004 OR PRY<2004 OR PY<2004 OR MY  
<2004 OR REVIEW/DT  
L24 17 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L23  
L27 271 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI (3A)  
(POST/OBI(W) PRANDIAL/OBI OR POSTPRANDIAL/OBI)  
L28 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND L27  
L29 13237 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI  
L30 13237 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 OR L29  
L31 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND L30  
L32 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 OR L31  
L33 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 OR L24

=> d his 149

(FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 14:54:53 ON 24 MAY 2007)

L49 33 S L48 (P) L13

=> d que 149

L4 1 SEA FILE=REGISTRY ABB=ON PLU=ON 145375-43-5/RN  
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON 207844-01-7/RN  
L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON MITIGLINIDE/CN  
L8 2 SEA FILE=REGISTRY ABB=ON PLU=ON (L4 OR L5 OR L6)  
L10 87 SEA FILE=HCAPLUS ABB=ON PLU=ON MITIGLINIDE/OBI OR MITI/OBI(W)  
GLINIDE/OBI  
L13 2160940 SEA FILE=HCAPLUS ABB=ON PLU=ON (INHIBIT?/OBI OR HINDER?/OBI  
OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR  
PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI)  
L19 110617 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABET?/OBI  
L23 QUE ABB=ON PLU=ON AY<2004 OR PRY<2004 OR PY<2004 OR MY  
<2004 OR REVIEW/DT  
L27 271 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI (3A)  
(POST/OBI(W) PRANDIAL/OBI OR POSTPRANDIAL/OBI)  
L29 13237 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI  
L43 84 SEA L8  
L44 172 SEA L10



10/519155

L45 10 SEA MITIGLINIDE CALCIUM HYDRATE  
L46 173 SEA (L43 OR L44 OR L45)  
L47 110 SEA L46 AND (L19 OR L27 OR L29)  
L48 46 SEA L47 AND L23  
L49 33 SEA L48 (P) L13

=> dup rem l33 l49

FILE 'HCAPLUS' ENTERED AT 15:07:58 ON 24 MAY 2007  
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PROCESSING COMPLETED FOR L33  
PROCESSING COMPLETED FOR L49

L61 49 DUP REM L33 L49 (8 DUPLICATES REMOVED)  
ANSWERS '1-24' FROM FILE HCAPLUS  
ANSWERS '25-42' FROM FILE MEDLINE  
ANSWERS '43-45' FROM FILE EMBASE  
ANSWERS '46-49' FROM FILE DRUGU

=> d l61 1-24 ibib ed abs hitind

L61 ANSWER 1 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2006:505268 HCAPLUS Full-text  
DOCUMENT NUMBER: 145:483552  
TITLE: Therapeutic efficacy of mitiglinide combined  
with once daily insulin glargine after switching from  
multiple daily insulin regimen of aspart insulin and  
glargine in patients with type 2 diabetes mellitus  
AUTHOR(S): Yoshihara, Tomoaki; Kumashiro, Naoki; Kanazawa,  
Yoshie; Mita, Tomoya; Sakurai, Yuko; Kawai, Junko;  
Abe, Michiko; Motojima, Kayoko; Hara, Kanako;  
Yamazaki, Yuka; Kanazawa, Akio; Miwa, Shinya; Sato,  
Fumihiko; Kanno, Rei; Shimizu, Tomoaki; Sakai, Ken;  
Uchino, Hiroshi; Watada, Hirotaka; Tanaka, Yasushi;  
Kawamori, Ryuzo; Hirose, Takahisa  
CORPORATE SOURCE: Department of Medicine, Metabolism and Endocrinology,  
School of Medicine, Juntendo University, Bunkyo-ku,  
Tokyo, 113-8421, Japan  
SOURCE: Endocrine Journal (Kyoto, Japan) (2006), 53(1), 67-72  
CODEN: ENJOEO; ISSN: 0918-8959  
PUBLISHER: Japan Endocrine Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
ED Entered STN: 31 May 2006  
AB Mitiglinide is novel class of rapid-acting insulin secretagogues, which have  
been widely used alone or in combination with other oral hypoglycemic drugs to  
improve postprandial hyperglycemia in early type 2 diabetes. While mitiglinide  
enhances postprandial requirement of insulin, the efficacy of mitiglinide

combined with insulin has yet to be established. We investigated the efficacy of mitiglinide combined with insulin glargine, the first soluble insulin analog that has a flat and prolonged effect. After control with the intensive regimen (daily aspart insulin and glargine), 30 inpatients with type 2 diabetes were switched to premeal mitiglinide combined with once daily insulin glargine (mitiglinide regimen), and daily profiles of blood glucose level were compared under each regimen. Fifteen patients showed similar control of hyperglycemia with mitiglinide regimen and intensive insulin regimen, assessed by M value ( $<32$ ), while the remaining 15 showed worsening under the mitiglinide regimen. The patients who were well controlled with mitiglinide regimen were significantly younger ( $51.9 \pm 16.0$  years,  $p < 0.005$ ) and heavier (body mass index:  $25.7 \pm 3.3$  kg/m<sup>2</sup>,  $p < 0.05$ ) than those who were not ( $67.9 \pm 8.7$  and  $23.0 \pm 3.1$ , resp.). Moreover, insulin doses of aspart per body weight were significantly fewer in effective group than in ineffective group. Duration of diabetes was shorter in the effective group, albeit insignificantly. Previous treatment before starting intensive insulin regimen, such as insulin and sulfonylurea, was not different between the two groups. Our results suggest that mitiglinide plus insulin glargine combination therapy is useful for lowering both fasting and postprandial hyperglycemia in a subpopulation of type 2 diabetes. The long-term effects of such treatment need to be established in future studies.

CC 1-10 (Pharmacology)

ST mitiglinide insulin glargine hyperglycemia type2  
diabetes mellitus antidiabetic

IT Antidiabetic agents

Body weight

Combination chemotherapy

Human

Hyperglycemia

(mitiglinide combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)

IT Glycerides, biological studies

High-density lipoproteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(mitiglinide combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)

IT Diabetes mellitus

(non-insulin-dependent; mitiglinide combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)

IT 50-99-7, D-Glucose, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(blood; mitiglinide combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)

IT 57-88-5, Cholesterol, biological studies 62572-11-6, Hemoglobin A1c

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(mitiglinide combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)

IT 9004-10-8, Insulin, biological studies 145375-43-5,

Mitiglinide 160337-95-1

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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitiglinide combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 2 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:962511 HCAPLUS Full-text

DOCUMENT NUMBER: 143:244659

TITLE: Method for examining blood glucose control state

INVENTOR(S): Kitahara, Yoshiro; Miura, Kyoko; Takeuchi, Masayoshi

PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005080993	A1	20050901	WO 2005-JP3438	20050223
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: JP 2004-47020 A 20040223

ED Entered STN: 02 Sep 2005

AB A novel diagnostic marker for a blood glucose control state is provided. Also provided is a method for diagnosing or examining a blood glucose control state. The method comprises a process for measuring the AGE2 concentration in a blood or body fluid sample of a patient by a measuring method selected from a Western blotting method, an enzyme immunoassay, a RIA, a liquid chromatog. and a dot blot method, and a process for evaluating the state of postprandial hyperglycemia control.

IC ICM G01N033-68

ICS G01N033-15; G01N033-50; G01N033-53; G01N033-577; G01N033-66

CC 9-10 (Biochemical Methods)

Section cross-reference(s): 14

IT Hyperglycemia

(postprandial; method for examining blood glucose control state by measuring blood AGE2)

IT 54870-28-9D, Meglitinide, derivative 105816-04-4, Nateglinide 135062-02-1, Repaglinide 145375-43-5, Mitiglinide

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(method for examining blood glucose control state by measuring blood AGE2)

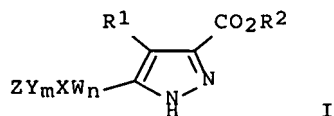
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 3 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

10/519155

ACCESSION NUMBER: 2005:120729 HCAPLUS Full-text  
DOCUMENT NUMBER: 142:219276  
TITLE: Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases  
INVENTOR(S): Semple, Graeme; Gharbaoui, Tawfik; Shin, Young-Jun; Decaire, Marc; Averbuj, Claudia; Skinner, Philip J.  
PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 130 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
WO 2005011677	A1	20050210	WO 2004-US18389	20040610 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004260636	A1	20050210	AU 2004-260636	20040610 <--
CA 2528834	A1	20050210	CA 2004-2528834	20040610 <--
EP 1633351	A1	20060315	EP 2004-776418	20040610 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007032537	A1	20070208	US 2006-560332	20060908 <--
PRIORITY APPLN. INFO.:			US 2003-478664P	P 20030613 <--
			WO 2004-US18389	W 20040610
OTHER SOURCE(S): MARPAT 142:219276				
ED Entered STN: 11 Feb 2005				
GI				



AB Title compds. [I; W, Y = (substituted) alkylene, alkenylene, alkynylene; X = NR3CO, NR3SO2, NR3, CO, CH(OH), C(NH), O, S, SO, SO2, etc.; R3, R4 = H, (substituted) alkyl, Ph, heteroaryl; Z = H, halo, (substituted) Ph, heteroaryl; R1 = H, OH, halo, alkyl, haloalkyl; R2 = H, alkyl; m, n = 0, 1; with provisos], were prepared Thus, 5-methylthiomethyl-2H-pyrazole-3-carboxylic acid (preparation outlined) showed hRUP25 agonist activity with EC50 = 4.3 µM.

IC ICM A61K031-415  
ICS C07D231-14; A61P003-06

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63

ST pyrazolecarboxylate prepn RUP25 nicotinic acid receptor agonist;  
dyslipidemia atherosclerosis heart disease diabetes obesity  
treatment pyrazolecarboxylate prepn

IT Diabetes mellitus  
(non-insulin-dependent, treatment; preparation of pyrazolecarboxylates as  
agonists for the RUP25 nicotinic acid receptor for the treatment of  
dyslipidemia and related diseases)

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 114-86-3, Phenformin  
339-43-5, Carbutamide 339-44-6, Glymidine 451-71-8, Glyhexamide  
535-65-9, Glybuthiazole 631-27-6, Glyclopamide 637-07-0, Clofibrate  
657-24-9, Metformin 664-95-9, Tolcyclamide 692-13-7, Buformin  
882-09-7, Clofibric acid 968-81-0, Acetohexamide 1156-19-0, Tolazamide  
1228-19-9, Glypinamide 1492-02-0, Glybuzole 3149-00-6, Phenbutamide  
3459-20-9, Glymidine 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8,  
Glibenclamide 14929-11-4, Simfibrate 21187-98-4, Gliclazide  
25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9,  
Glibornuride 29094-61-9, Glipizide 30299-08-2, Clinofibrate  
31637-97-5, Etofibrate 31980-29-7, Nicofibrate 33342-05-1, Gliquidone  
41859-67-0, Bezafibrate 42597-57-9, Ronifibrate, biological studies  
49562-28-9, Fenofibrate 52214-84-3, Ciprofibrate 54504-70-0,  
Theofibrate 55285-45-5, Pirifibrate 55937-99-0, Beclobrate  
56180-94-0, Acarbose 62571-86-2, Captopril 68367-52-2, Sorbinil  
69047-39-8, Binifibrate 72432-03-2, Miglitol 74258-86-9, Alacepril  
75330-75-5, Lovastatin 75847-73-3, Enalapril 76420-72-9, Enalaprilat  
76547-98-3, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin  
82159-09-9, Epalrestat 82834-16-0, Perindopril 82964-04-3, Tolrestat  
83435-66-9, Delapril 83480-29-9, Voglibose 83647-97-6, Spirapril  
85441-61-8, Quinapril 85856-54-8, Moveltipril 86541-75-5, Benazepril  
87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5, Cilazapril  
89371-37-9, Imidapril 89391-50-4, Imirestat 93479-97-1, Glimepiride  
93957-54-1, Fluvastatin 98048-97-6, Fosinopril 105816-04-4,  
Nateglinide 110703-94-1, Zopolrestat 111025-46-8, Pioglitazone  
111223-26-8, Ceronapril 111902-57-9, Temocapril 112733-06-9,  
Zenarestat 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin  
145375-43-5, Mitiglinide 145599-86-6, Cerivastatin  
287714-41-4, Rosuvastatin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(coadministration; preparation of pyrazolecarboxylates as agonists for the  
RUP25 nicotinic acid receptor for the treatment of dyslipidemia and  
related diseases)

IT 9001-42-7,  $\alpha$ -Glucosidase 9028-31-3, Aldose reductase  
9028-35-7, Hmg coa reductase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors coadministration; preparation of pyrazolecarboxylates  
as agonists for the RUP25 nicotinic acid receptor for the treatment of  
dyslipidemia and related diseases)

IT 9015-82-1

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors, coadministration; preparation of pyrazolecarboxylates  
as agonists for the RUP25 nicotinic acid receptor for the treatment of  
dyslipidemia and related diseases)

IT 111-02-4, Squalene

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(synthesis inhibitors coadministration; preparation of  
pyrazolecarboxylates as agonists for the RUP25 nicotinic acid receptor  
for the treatment of dyslipidemia and related diseases)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 4 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1009580 HCAPLUS Full-text

DOCUMENT NUMBER: 144:142642

TITLE: Effects of S21403 (mitiglinide) on postprandial generation of oxidative stress and inflammation in type 2 diabetic patients

AUTHOR(S): Assaloni, R.; Ros, R. Da; Quagliaro, L.; Piconi, L.; Maier, A.; Zuodar, G.; Motz, E.; Ceriello, A.

CORPORATE SOURCE: Department of Pathology and Medicine, Experimental and Clinical, University of Udine, Udine, Italy

SOURCE: Diabetologia (2005), 48(9), 1919-1924  
CODEN: DBTGAI; ISSN: 0012-186X

PUBLISHER: Springer GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 19 Sep 2005

AB Aim/hypothesis: Evidence suggests that postprandial hyperglycemia may be a cardiovascular risk factor in diabetes. Oxidative stress and inflammation are involved in the pathogenesis of diabetic complications and previous studies have shown increased oxidative stress and inflammation in the postprandial phase in diabetic patients. The aim of the present study was to evaluate whether controlling postprandial hyperglycemia with S21403 (mitiglinide) is accompanied by a reduced generation of oxidative stress and inflammation. Subjects and methods: Forty type 2 diabetic patients participated in the study. Two different breakfast-tests were performed in each patient, with placebo or S21403. Plasma nitrotyrosine, plasma malondialdehyde (MDA), oxidized LDL (oxLDL), plasma total radical-trapping antioxidant parameter (TRAP), IL-6, IL-18, TNF- $\alpha$ , plasma glucose and insulin were measured. Results: After the administration of S21403, 40 mg, a rapid stimulation of insulin secretion was observed, accompanied by a reduction of postprandial hyperglycemia. With S21403, a significant decrease of either nitrotyrosine, MDA and oxLDL levels, and a preservation of plasma TRAP compared with placebo was found. Significant decreases of IL-6, IL-18 and TNF- $\alpha$  were also observed with S21403 compared with placebo. Conclusions/interpretation: This study shows that controlling postprandial hyperglycemia with S21403 significantly improves the cluster of oxidative stress and inflammation markers that are increased in the postprandial state in diabetic patients.

CC 1-10 (Pharmacology)

ST **mitiglinide postprandial hyperglycemia**

oxidative stress inflammation diabetes antidiabetic

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (SSR (signal sequence receptor); controlling **postprandial hyperglycemia** with S21403 significantly decreased oxidative stress markers nitrotyrosine, MDA, oxLDL levels and preserved plasma TRAP in type 2 diabetic patient)

IT Interleukin 18

RL: BSU (Biological study, unclassified); BIOL (Biological study) (controlling **postprandial hyperglycemia** with S21403 significantly decreased inflammatory marker interleukin-18 in type 2 diabetic patient)

IT Interleukin 6

RL: BSU (Biological study, unclassified); BIOL (Biological study) (controlling **postprandial hyperglycemia** with S21403 significantly decreased inflammatory marker interleukin-6 in type 2 diabetic patient)

IT Tumor necrosis factors

- RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(controlling **postprandial hyperglycemia** with S21403  
significantly decreased inflammatory marker tumor necrosis  
factor- $\alpha$  in type 2 diabetic patient)
- IT Inflammation  
(controlling **postprandial hyperglycemia** with S21403  
significantly decreased inflammatory markers IL-6, IL-18, TNF- $\alpha$   
in type 2 diabetic patient)
- IT Human  
**Hyperglycemia**  
**Pancreas**  
(controlling **postprandial hyperglycemia** with S21403  
significantly decreased oxidative stress markers nitrotyrosine, MDA,  
oxLDL levels, inflammatory markers IL-6, IL-18, TNF- $\alpha$  and  
preserved plasma TRAP in type 2 diabetic patient)
- IT Oxidative stress, biological  
(controlling **postprandial hyperglycemia** with S21403  
significantly decreased oxidative stress markers nitrotyrosine,  
malondialdehyde, oxLDL levels and preserved plasma TRAP in type 2  
diabetic patient)
- IT Antidiabetic agents  
(controlling **postprandial hyperglycemia** with  
**mitiglinide** significantly decreased oxidative stress markers  
nitrotyrosine, MDA, oxLDL levels, inflammatory markers IL-6, IL-18,  
TNF- $\alpha$  and preserved plasma TRAP in type 2 diabetic patient)
- IT Diabetes mellitus  
(non-insulin-dependent; controlling **postprandial**  
**hyperglycemia** with S21403 significantly decreased oxidative  
stress markers nitrotyrosine, MDA, oxLDL levels, inflammatory markers  
IL-6, IL-18, TNF- $\alpha$  and preserved plasma TRAP in type 2 diabetic  
patient)
- IT Low-density lipoproteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(oxidized; controlling **postprandial hyperglycemia**  
with S21403 significantly decreased oxidative stress marker oxLDL  
levels in type 2 diabetic patient)
- IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological  
studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(S21403 stimulated insulin secretion which was accompanied by reduction of  
**postprandial hyperglycemia** in type 2 diabetic  
patient)
- IT 542-78-9, Malondialdehyde  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(controlling **postprandial hyperglycemia** with S21403  
significantly decreased oxidative stress marker malondialdehyde in type  
2 diabetic patient)
- IT 621-44-3  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(controlling **postprandial hyperglycemia** with S21403  
significantly decreased oxidative stress marker nitrotyrosine in type 2  
diabetic patient)
- IT 145375-43-5, Mitiglinide  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(controlling **postprandial hyperglycemia** with  
**mitiglinide** significantly decreased oxidative stress markers  
nitrotyrosine, MDA, oxLDL levels, inflammatory markers IL-6, IL-18,  
TNF- $\alpha$  and preserved plasma TRAP in type 2 diabetic patient)

10/519155

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 5 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2004:902180 HCAPLUS Full-text  
DOCUMENT NUMBER: 141:355415  
TITLE: A synergistic pharmaceutical combination comprising  
cicletanine for the prevention or treatment  
of diabetes  
INVENTOR(S): Egri, Janos  
PATENT ASSIGNEE(S): Synosens Kutato es Fejlesztő Kft., Hung.  
SOURCE: PCT Int. Appl., 29 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091612	A1	20041028	WO 2004-HU37	20040414 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 200300990	A2	20050530	HU 2003-990	20030415 <--
CA 2522126	A1	20041028	CA 2004-2522126	20040414 <--
EP 1648453	A1	20060426	EP 2004-727331	20040414 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2006523668	T	20061019	JP 2006-506248	20040414 <--
PRIORITY APPLN. INFO.:			HU 2003-990	A 20030415 <--
			WO 2004-HU37	W 20040414

OTHER SOURCE(S): MARPAT 141:355415

ED Entered STN: 28 Oct 2004

AB The invention refers to a synergistic pharmaceutical combination comprising  
(a) a first pharmaceutical composition containing cicletanine or a  
pharmaceutically suitable acid addition salt thereof and one or more  
conventional carrier(s), and (b) a second pharmaceutical composition  
containing an antidiabetic or antihyperlipidemic active agent or, if desired  
and chemical possible, a pharmaceutically suitable acid addition salt or a  
salt formed with a pharmaceutically suitable base thereof and one or more  
conventional carrier(s). An antidiabetic agent is selected from a  
thiazolidinedione derivative, a sulfonylurea, or a biguanidine derivative. The  
pharmaceutical combination is suitable for the prevention or treatment of a  
prediabetic state, metabolic X-syndrome or diabetes mellitus, as well as  
disorders associated with these states.

IC ICM A61K031-4355

ICS A61K031-155; A61K031-427; A61K031-64; A61P003-00; A61P003-10

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 2

ST cicletanine antidiabetic hypolipemic synergy diabetes  
complication



- IT Hair, disease  
(diffuse effluvium; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Metabolic disorders  
(metabolic syndrome X; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Antidiabetic agents  
(oral; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Ovary, disease  
(polycystic; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Alopecia  
Antidiabetic agents  
Combination chemotherapy  
Diabetes mellitus  
Hypolipemic agents  
(synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Dyslipidemia  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Sulfonylureas  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Drug interactions  
(synergistic; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT 10238-21-8, Glyburide  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Glibenclamide; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(resistance; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT 64-77-7, Tolbutamide 94-20-2, Chloropropamide 114-86-3, Phenformin 631-27-6, Glycropyramide 637-07-0, Clofibrate 657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1492-02-0, Glybuzole 2295-31-0D, Thiazolidinedione, derivs. 5868-05-3, Niceritrol 6882-47-9D, Biguanidine, derivs. 10571-59-2, Nicoclonate 11041-12-6, Cholestyramine 14929-11-4, Simfibrate 21187-98-4, Glliclazide 24477-37-0, Glisolamide 25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9, Glibornuride 27959-26-8, Nicomol 29094-61-9, Glipizide 31637-97-5, Etofibrate 32797-92-5, Glisentide 33342-05-1, Gliquidone 42597-57-9, Ronifibrate, biological studies 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 56180-94-0, Acarbose 56227-39-5, Polidexide 72432-03-2, Miglitol 74772-77-3, Ciglitazone 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82747-56-6, Cicletanine hydrochloride

10/519155

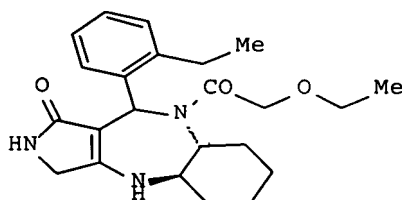
83480-29-9, Voglibose 89943-82-8, Cicletanine 93479-97-1, Glimepiride  
93957-54-1, Fluvastatin 97322-87-7, Troglitazone 105816-04-4,  
Senaglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone  
134523-00-5, Atorvastatin 135062-02-1, Repaglinide 145375-43-5  
, Mitiglinide

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(synergistic combination comprising cicletanine for prevention  
or treatment of diabetes and related disorders)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 6 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2004:681582 HCAPLUS Full-text  
DOCUMENT NUMBER: 141:185111  
TITLE: Remedy for diabetes  
INVENTOR(S): Ikenoue, Takao; Kageyama, Yoko; Iino, Yukio; Kondo,  
Nobuo  
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan  
SOURCE: PCT Int. Appl., 49 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069259	A1	20040819	WO 2004-JP1279	20040206 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004210268	A1	20040819	AU 2004-210268	20040206 <--
CA 2515294	A1	20040819	CA 2004-2515294	20040206 <--
EP 1595544	A1	20051116	EP 2004-708897	20040206 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007303	A	20060207	BR 2004-7303	20040206 <--
CN 1771040	A	20060510	CN 2004-80009410	20040206 <--
US 2005272641	A1	20051208	US 2005-198511	20050808 <--
PRIORITY APPLN. INFO.:			JP 2003-31088	A 20030207 <--
			WO 2004-JP1279	A 20040206
OTHER SOURCE(S): MARPAT 141:185111				
ED Entered STN: 20 Aug 2004				
GI				



AB A preventive and/or a remedy for diabetes, diabetic complications, hyperinsulinemia, sugar metabolic error or obesity characterized by comprising a combination of a compound represented by the following formula (I; Markush's structures given), its analog or a pharmaceutically acceptable salt thereof with a hypoglycemic agent.

IC ICM A61K031-5517  
ICS A61K031-551; A61K031-553; A61K031-554; A61P003-04; A61P003-10; A61P043-00; A61K045-00; C07D487-04

CC 1-10 (Pharmacology)  
Section cross-reference(s): 2

IT Nerve, disease  
(diabetic neuropathy; heterocyclic compds. as antidiabetic and antiobesity agents)

IT Antidiabetic agents  
Antihypertensives  
Antiobesity agents  
Antioxidants  
Diabetes mellitus  
Drug resistance  
Obesity  
 $\beta$ 3-Adrenoceptor agonists  
(heterocyclic compds. as antidiabetic and antiobesity agents)

IT 56-03-1D, Biguanide, derivs. 114-86-3, Fenformin 657-24-9, Metformin 692-13-7, Buformin 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 56180-94-0, Acarbose 105816-04-4, Nateglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 145375-43-5, Mitiglinide 433729-78-3 433729-79-4 433729-80-7 433729-81-8 433729-82-9 433729-83-0 433729-84-1 433729-85-2 433729-86-3 433729-87-4 433729-88-5 433729-89-6 433729-90-9 433729-91-0 433729-92-1 433729-93-2 433729-94-3 433729-95-4 433729-96-5 433729-97-6 433729-98-7 433729-99-8 433730-00-8 433730-01-9 433730-02-0 433730-03-1 433730-04-2 433730-05-3 433730-06-4 433730-07-5 433730-08-6 433730-09-7 433730-10-0 433730-11-1 433730-12-2 433730-13-3 433730-14-4 433730-15-5 433730-16-6 433730-17-7 433730-18-8 433730-19-9 433730-20-2 433730-21-3 433730-22-4 433730-23-5 433730-24-6 433730-25-7 433730-26-8 433730-27-9 433730-28-0 433730-29-1 433730-30-4 433730-31-5 433730-32-6 433730-33-7 433730-34-8 433730-35-9 433730-36-0 433730-37-1 433730-38-2 433730-39-3 433730-40-6 433730-41-7 433730-42-8 433730-43-9 433730-44-0 433730-45-1 433730-46-2 433730-47-3 433730-48-4 433730-49-5 433730-50-8 433730-51-9 433730-52-0 433730-53-1 433730-54-2 433730-55-3 433730-56-4 433730-57-5 433730-58-6 433730-59-7 433730-60-0 433730-61-1 433730-62-2 433730-63-3 433730-64-4 433730-65-5 433730-66-6 433730-67-7 433730-68-8 433730-69-9 433730-70-2 433730-72-4 433730-73-5 433730-75-7 433730-76-8 433730-77-9 433730-78-0 433730-79-1 433730-80-4 433730-81-5 433730-82-6 433730-83-7 433730-84-8 433730-85-9 433730-86-0 433730-87-1 433730-88-2 433730-89-3 433730-90-6 433730-91-7 433730-92-8 433730-93-9 433730-94-0 433730-95-1 433730-96-2 433730-97-3 433730-98-4 433730-99-5 433731-00-1 433731-01-2 433731-02-3 433731-04-5 433731-06-7 433731-08-9 433731-09-0 433731-10-3 433731-11-4 737804-07-8 737804-08-9 737804-09-0 737804-10-3 737804-11-4 737804-12-5 737804-13-6 737804-14-7 737804-15-8 737804-16-9 737804-17-0 737804-18-1 737804-19-2 737804-20-5 737804-21-6 737804-22-7 737804-23-8 737804-24-9 737804-25-0

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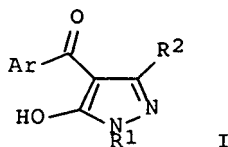
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(heterocyclic compds. as antidiabetic and antiobesity agents)

IT 9001-62-1, Lipase 9028-31-3, Aldose reductase 9035-74-9,  
Glycogen phosphorylase 54249-88-6, Dipeptidyl peptidase IV  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; heterocyclic compds. as antidiabetic and  
antiobesity agents)

L61 ANSWER 7 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2004:333698 HCAPLUS Full-text  
DOCUMENT NUMBER: 140:357333  
TITLE: Preparation of aroylhydroxypyrazoles for treatment of  
metabolic disorders  
INVENTOR(S): Semple, Graeme; Shin, Young Jun  
PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 125 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033431	A2	20040422	WO 2003-US31509	20031002 <--
WO 2004033431	A3	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003282679	A1	20040504	AU 2003-282679	20031002 <--
PRIORITY APPLN. INFO.:			US 2002-416193P	P 20021004 <--
			US 2002-417120P	P 20021007 <--
			WO 2003-US31509	W 20031002 <--

OTHER SOURCE(S): MARPAT 140:357333  
ED Entered STN: 23 Apr 2004  
GI



AB Title compds. [I; R1 = alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, benzyl,  
optionally substituted with  $\geq 1$  halo, OH, cyano, NO<sub>2</sub>, haloalkyl, amino,  
aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl,

alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfinyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalkylsulfonyl, alkylureyl, arylureyl; R2 = H, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, PhCH2, Ph, heteroaryl, optionally substituted with  $\geq 1$  halo, OH, cyano, nitro, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl, alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfonyl, alkylsulfinyl, haloalkylthio, haloalkylsulfinyl, haloalkylsulfonyl, alkylureyl or arylureyl groups; Ar = (substituted) pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, were prepared for the treatment of metabolic-related disorders, including dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, type 2 diabetes, Syndrome-X and the like (no data). Thus, nicotiny chloride, 2-methyl-5-propyl-2,4-dihydropyrazol-3-one, and Ca(OH)<sub>2</sub> were heated at 90° in dioxane for 2 h. to give (5-hydroxy-1-methyl-3-propyl-1H-pyrazol-4-yl)pyridin-3-ylmethanone. I may be used in combination with other active agents such  $\alpha$ -glucosidase inhibitors, aldose reductase inhibitors, biguanides, HMG-CoA reductase inhibitors, squalene synthesis inhibitors, fibrates, LDL catabolism enhancers, angiotensin converting enzyme inhibitors, and insulin secretion enhancers.

IC ICM C07D231-00

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT Diabetes mellitus

(non-insulin-dependent; preparation of aroylhydroxypyrazoles for treatment of metabolic disorders)

IT 56-03-1, Biguanide 64-77-7, Tolbutamide 94-20-2, Chloropropamide 114-86-3, Phenformin 339-43-5, Carbutamide 339-44-6, Glymidine 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6, Glyclopamide 637-07-0, Clofibrate 657-24-9, Metformin 664-95-9, Tolcyclamide 692-13-7, Buformin 882-09-7, Clofibric acid 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybuzole 2295-31-0D, Thiazolidinedione, derivs 3149-00-6, Phenbutamide 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 14929-11-4, Simfibrate 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9, Glibornuride 29094-61-9, Glipizide 30299-08-2, Clinofibrate 31637-97-5, Etofibrate 31980-29-7, Nicofibrate 33342-05-1, Gliquidone 41859-67-0, Bezafibrate 42597-57-9, Ronifibrate, biological studies 49562-28-9, Fenofibrate 52214-84-3, Ciprofibrate 54504-70-0, Theofibrate 55285-45-5, Pirifibrate 55937-99-0, Beclobrate 56180-94-0, Acarbose 62571-86-2, Captopril 68367-52-2, Sorbinil 69047-39-8, Binifibrate 74258-86-9, Alacepril 75330-75-5, Lovastatin 75847-73-3, Enalapril 76420-72-9, Enalaprilat 76547-98-3, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82159-09-9, Epalrestat 82834-16-0, Perindopril 82964-04-3, Tolrestat 83435-66-9, Delapril 83480-29-9, Voglibose 83647-97-6, Spirapril 85441-61-8, Quinapril 85856-54-8, Moveltipril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5, Cilazapril 89371-37-9, Imidapril 89391-50-4, Imirestat 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 98048-97-6, Fosinopril 105816-04-4, Nateglinide 110703-94-1, Zopolrestat 111025-46-8, Pioglitazone 111223-26-8, Ceronapril 111902-57-9, Temocapril 112733-06-9, Zenarestat 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 145375-43-5, Mitiglinide 145599-86-6, Cerivastatin 287714-41-4, Rosuvastatin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(coadministration; preparation of aroylhydroxypyrazoles for treatment of metabolic disorders)

IT 9001-42-7,  $\alpha$ -Glucosidase 9015-82-1, Angiotensin converting enzyme

10/519155

9028-31-3, Aldose reductase 9028-35-7, HMG-CoA  
reductase 9077-14-9, Squalene synthase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors coadministration; preparation of aroylhydroxypyrazoles  
for treatment of metabolic disorders)

L61 ANSWER 8 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:60541 HCAPLUS Full-text

DOCUMENT NUMBER: 140:105298

TITLE: Bicyclic oligopeptides and their use as glucagon  
receptor antagonists

INVENTOR(S): Potterat, Olivier; Streicher, Ruediger; Wagner, Klaus;  
Maurer, Till; Mack, Juergen; Peters, Stefan

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
WO 2004007535	A1	20040122	WO 2003-EP7657	20030715 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2489189	A1	20040122	CA 2003-2489189	20030715 <--
AU 2003246702	A1	20040202	AU 2003-246702	20030715 <--
EP 1525218	A1	20050427	EP 2003-763864	20030715 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2006505507	T	20060216	JP 2004-520641	20030715 <--
US 2004072736	A1	20040415	US 2003-621272	20030717 <--
US 7101848	B2	20060905		
PRIORITY APPLN. INFO.:			EP 2002-15907	A 20020717 <--
			US 2002-416797P	P 20021008 <--
			WO 2003-EP7657	W 20030715 <--

OTHER SOURCE(S): MARPAT 140:105298

ED Entered STN: 26 Jan 2004

AB The invention relates to a bicyclic oligopeptide or ester thereof having the capability to inhibit the glucagon receptor, which essentially consists of (a) a first cyclic group, which comprises at least one cysteine group and is formed by an amide bonding of the N-terminal amino acid with the second carboxylate group of a diacid amino acid, and (b) a second cyclic group which is formed by an amide bonding of an amino acid with the -carboxylate group of said diacid amino acid, and by a disulfide bonding of the C-terminal cysteine and a cysteine group within the first cyclic group (a); and to the use of such bicyclic oligopeptides for the preparation of a medicament for the treatment or prevention of diseases, in which glucagon receptors are involved.

IC ICM C07K007-56

ICS A61K038-12; C07K014-36

CC 1-10 (Pharmacology)

Section cross-reference(s): 2, 10, 34, 63

- ST bicyclic oligopeptide glucagon receptor **inhibition** disease treatment; **diabetes** treatment bicyclic oligopeptide glucagon receptor **inhibition**
- IT Proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ALBP (adipocyte lipid-binding protein), **inhibitors**; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Streptomyces  
(DSM 14996, bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Transport proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SGLT2 (sodium-dependent glucose transporter 2), **inhibitors**; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Glucagon-like peptide-1 receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (agonists; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems  
(ampoules; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Actinomyces  
(bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Antidiabetic agents  
Antiobesity agents  
Cardiovascular agents  
**Diabetes** mellitus  
Human  
Peroxisome proliferators  
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Glucagon receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems  
(capsules; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems  
(carriers; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Peptides, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cyclic; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and

- metabolic stability)
- IT Lipids, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (modulating agents; bicyclic oligopeptides as glucagon receptor  
**inhibitors** in relation to disease treatment and combination  
 with other agents and metabolic stability)
- IT Retinoid X receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (modulators; bicyclic oligopeptides as glucagon receptor  
**inhibitors** in relation to disease treatment and combination  
 with other agents and metabolic stability)
- IT Drug delivery systems  
 (suppositories; bicyclic oligopeptides as glucagon receptor  
**inhibitors** in relation to disease treatment and combination  
 with other agents and metabolic stability)
- IT Drug delivery systems  
 (tablets, coated; bicyclic oligopeptides as glucagon receptor  
**inhibitors** in relation to disease treatment and combination  
 with other agents and metabolic stability)
- IT Drug delivery systems  
 (tablets; bicyclic oligopeptides as glucagon receptor  
**inhibitors** in relation to disease treatment and combination  
 with other agents and metabolic stability)
- IT Peroxisome proliferator-activated receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 ( $\alpha$ , modulators; bicyclic oligopeptides as glucagon receptor  
**inhibitors** in relation to disease treatment and combination  
 with other agents and metabolic stability)
- IT Peroxisome proliferator-activated receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 ( $\gamma$ , modulators; bicyclic oligopeptides as glucagon receptor  
**inhibitors** in relation to disease treatment and combination  
 with other agents and metabolic stability)
- IT 145375-43-5, Mitiglinide  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (analogs; bicyclic oligopeptides as glucagon receptor  
**inhibitors** in relation to disease treatment and combination  
 with other agents and metabolic stability)
- IT 9007-92-5, Glucagon, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (bicyclic oligopeptides as glucagon receptor **inhibitors** in  
 relation to disease treatment and combination with other agents and  
 metabolic stability)
- IT 647807-35-0P  
 RL: BSU (Biological study, unclassified); NPO (Natural product  
 occurrence); PAC (Pharmacological activity); PUR (Purification or  
 recovery); THU (Therapeutic use); BIOL (Biological study); OCCU  
 (Occurrence); PREP (Preparation); USES (Uses)  
 (bicyclic oligopeptides as glucagon receptor **inhibitors** in  
 relation to disease treatment and combination with other agents and  
 metabolic stability)
- IT 647807-36-1P  
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
 SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (bicyclic oligopeptides as glucagon receptor **inhibitors** in  
 relation to disease treatment and combination with other agents and  
 metabolic stability)
- IT 9004-10-8, Insulin, biological studies



10/519155

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(bicyclic oligopeptides as glucagon receptor inhibitors in  
relation to disease treatment and combination with other agents and  
metabolic stability)

IT 56-03-1D, Biguanide, derivs. 94-20-2, Chloropropamide 657-24-9,  
Metformin 10238-21-8, Glyburide 21187-98-4, Gliclazide 29094-61-9,  
Glipizide 56180-94-0, Acarbose 72432-03-2, Miglitol 89750-14-1,  
Glucagon-like peptide I 93479-97-1, Glimepiride 97322-87-7,  
Troglitazone 105816-04-4, Nateglinide 111025-46-8, Pioglitazone  
122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 141732-76-5,  
Exendin-4 161600-01-7, Isaglitazone

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(bicyclic oligopeptides as glucagon receptor inhibitors in  
relation to disease treatment and combination with other agents and  
metabolic stability)

IT 9033-06-1, Glucosidase 54249-88-6, Dipeptidyl peptidase IV  
300865-11-6, Protein tyrosine phosphatase 1B 391208-93-8, Glycogen  
synthase kinase 3

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; bicyclic oligopeptides as glucagon receptor  
inhibitors in relation to disease treatment and combination  
with other agents and metabolic stability)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 9 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:60532 HCAPLUS Full-text

DOCUMENT NUMBER: 140:105297

TITLE: Bicyclic oligopeptides and their use as glucagon  
receptor antagonists

INVENTOR(S): Potterat, Olivier; Streicher, Ruediger; Wagner, Klaus;  
Maurer, Till; Mack, Juergen; Peters, Stefan

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007524	A2	20040122	WO 2003-EP7311	20030708 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003260306	A1	20040202	AU 2003-260306	20030708 <--
US 2004072736	A1	20040415	US 2003-621272	20030717 <--
US 7101848	B2	20060905		
PRIORITY APPLN. INFO.:			EP 2002-15907	A 20020717 <--
			US 2002-416797P	P 20021008 <--

OTHER SOURCE(S): MARPAT 140:105297

ED Entered STN: 26 Jan 2004

AB The invention relates to a bicyclic oligopeptide or ester thereof having the capability to inhibit the glucagon receptor, which essentially consists of (a) a first cyclic group, which comprises at least one cysteine group and is formed by an amide bonding of the N-terminal amino acid with the second carboxylate group of a diacid amino acid, and (b) a second cyclic group which is formed by an amide bonding of an amino acid with the -carboxylate group of said diacid amino acid, and by a disulfide bonding of the C-terminal cysteine and a cysteine group within the first cyclic group (a); and to the use of such bicyclic oligopeptides for the preparation of a medicament for the treatment or prevention of diseases, in which glucagon receptors are involved.

IC ICM C07K

CC 1-10 (Pharmacology)

Section cross-reference(s): 10, 34, 63

ST bicyclic oligopeptide glucagon receptor inhibition disease treatment; diabetes treatment bicyclic oligopeptide glucagon receptor inhibition

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (ALBP (adipocyte lipid-binding protein), inhibitors; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Streptomyces

(DSM 14996, bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Transport proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (SGLT2 (sodium-dependent glucose transporter 2), inhibitors; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Glucagon-like peptide-1 receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (agonists; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems

(ampoules; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Actinomyces

(bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Antidiabetic agents

Antiobesity agents

Cardiovascular agents

Diabetes mellitus

Human

(bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Glucagon receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and

- metabolic stability)
- IT Drug delivery systems  
(capsules; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems  
(carriers; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Peptides, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cyclic; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Lipids, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(modulating agents; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Retinoid X receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(modulators; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems  
(suppositories; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems  
(tablets, coated; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems  
(tablets; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Peroxisome proliferator-activated receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
( $\alpha$ , agonists; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT Peroxisome proliferator-activated receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
( $\gamma$ , modulators; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT 145375-43-5, Mitiglinide  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(analogs; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT 9007-92-5, Glucagon, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
- IT 647807-35-0P  
RL: BSU (Biological study, unclassified); NPO (Natural product

occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)

(bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT 647807-36-1P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT 9004-10-8, Insulin, biological studies

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT 56-03-1D, Biguanide, derivs. 94-20-2, Chloropropamide 657-24-9, Metformin 10238-21-8, Glyburide 21187-98-4, Gliclazide 29094-61-9, Glipizide 56180-94-0, Acarbose 72432-03-2, Miglitol 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 97322-87-7, Troglitazone 105816-04-4, Nateglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 141732-76-5, Exendin-4 161600-01-7, Isaglitazone

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT 9033-06-1, Glucosidase 54249-88-6, Dipeptidyl peptidase IV 300865-11-6, Protein tyrosine phosphatase 1B 391208-93-8, Glycogen synthase kinase 3

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

L61 ANSWER 10 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:20487 HCAPLUS Full-text

DOCUMENT NUMBER: 140:65256

TITLE: Drug composition for prevention or inhibition of advance of diabetic complication

INVENTOR(S): Mikoshiba, Imao; Suzuki, Hisao; Kiyono, Yuji

PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002474	A1	20040108	WO 2003-JP8084	20030626 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,			

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LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,  
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
CA 2489660 A1 20040108 CA 2003-2489660 20030626 <--  
AU 2003244083 A1 20040119 AU 2003-244083 20030626 <--  
EP 1552830 A1 20050713 EP 2003-761816 20030626 <--  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
CN 1665499 A 20050907 CN 2003-815245 20030626 <--  
US 2005215607 A1 20050929 US 2004-519155 20041227 <--  
PRIORITY APPLN. INFO.: JP 2002-189559 A 20020628 <--  
WO 2003-JP8084 W 20030626 <--  
ED Entered STN: 11 Jan 2004  
AB Disclosed is a drug composition capable of attaining a good state of blood  
sugar control so as to enable correcting postprandial high blood sugar levels  
or high blood sugar levels at early fasting time. In particular, a drug  
composition for prevention or inhibition of advance of diabetic complications  
to be taken before meals, comprising 5 to 45 mg, in terms of one-time dose, of  
mitiglinide or its pharmacol. acceptable salt or a hydrate thereof, e.g.,  
mitiglinide calcium salt hydrate. The drug composition is highly useful for  
the prevention or inhibition of advance of, for example, diabetic microangio  
complications and arteriosclerosis because the ratio of occurrence of side  
effects, such as low blood sugar level symptom and gastrointestinal tract  
disorder, is low. A tablet containing mitiglinide calcium salt hydrate 10  
mg/tablet was formulated, and its effect on blood sugar level and side effect  
in patients with type 2 biabetes was examined  
IC ICM A61K031-4035  
ICS A61P003-10; A61P009-00; A61P009-10; A61P013-12; A61P027-02;  
A61P043-00  
CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1  
ST mitiglinide diabetic complication treatment oral  
IT Blood vessel, disease  
(diabetic microangiopathy; drug composition for prevention  
or inhibition of advance of diabetic complication)  
IT Kidney, disease  
(diabetic nephropathy; drug composition for prevention  
or inhibition of advance of diabetic complication)  
IT Eye, disease  
(diabetic retinopathy; drug composition for prevention  
or inhibition of advance of diabetic complication)  
IT Arteriosclerosis  
(diabetic; drug composition for prevention or  
inhibition of advance of diabetic complication)  
IT Human  
(drug composition for prevention or inhibition of  
advance of diabetic complication)  
IT Diabetes mellitus  
(non-insulin-dependent; drug composition for prevention or  
inhibition of advance of diabetic complication)  
IT Antidiabetic agents  
(oral; drug composition for prevention or inhibition of  
advance of diabetic complication)  
IT Drug delivery systems  
(tablets; drug composition for prevention or inhibition  
of advance of diabetic complication)

10/519155

IT 50-99-7, D-Glucose, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(blood; drug composition for **prevention or inhibition** of  
advance of **diabetic** complication)  
IT 145375-43-5, Mitiglinide 207844-01-7  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(drug composition for **prevention or inhibition** of  
advance of **diabetic** complication)  
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 11 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2004:20486 HCAPLUS Full-text  
DOCUMENT NUMBER: 140:65255  
TITLE: Drug composition for blood sugar control  
INVENTOR(S): Mikoshiba, Imao; Suzuki, Hisao; Kiyono, Yuji  
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 22 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004002473	A1	20040108	WO 2003-JP8083	20030626
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2490250	A1	20040108	CA 2003-2490250	20030626
AU 2003244082	A1	20040119	AU 2003-244082	20030626
EP 1532979	A1	20050525	EP 2003-761815	20030626
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1665498	A	20050907	CN 2003-815244	20030626
US 2005267195	A1	20051201	US 2004-519102	20041227
PRIORITY APPLN. INFO.:			JP 2002-189556	A 20020628
			WO 2003-JP8083	W 20030626

ED Entered STN: 11 Jan 2004

AB Disclosed is a drug composition capable of attaining a good state of blood sugar control so as to enable correcting postprandial high blood sugar levels or high blood sugar levels at early fasting time. In particular, a drug composition for blood sugar control to be taken before meals, comprising 5 to 45 mg, in terms of one-time dose, of mitiglinide or its pharmacol. acceptable salt or a hydrate thereof, e.g., mitiglinide calcium salt hydrate. The drug composition is highly useful for the prevention and treatment of, for example, type 2 diabetes because the ratio of occurrence of side effects, such as low blood sugar level symptom and gastrointestinal tract disorder, is low. A tablet containing mitiglinide calcium salt hydrate 10 mg/tablet was formulated, and its effect on blood sugar level and side effect in patients with type 2 diabetes was examined

IC ICM A61K031-4035  
 ICS A61P003-10; A61P043-00  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1  
 ST **mitiglinide** oral type 2 antidiabetic  
 IT Human  
     **Hyperglycemia**  
     (drug composition for blood sugar control containing **mitiglinide**)  
 IT Diabetes mellitus  
     (non-insulin-dependent; drug composition for blood sugar control containing  
     **mitiglinide**)  
 IT Antidiabetic agents  
     (oral; drug composition for blood sugar control containing **mitiglinide**  
     )  
 IT Drug delivery systems  
     (tablets; drug composition for blood sugar control containing  
     **mitiglinide**)  
 IT 50-99-7, D-Glucose, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (blood; drug composition for blood sugar control containing **mitiglinide**  
     )  
 IT 145375-43-5, **Mitiglinide** 207844-01-7  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
     (Biological study); USES (Uses)  
     (drug composition for blood sugar control containing **mitiglinide**)  
 REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 12 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2004:496322 HCAPLUS Full-text  
 DOCUMENT NUMBER: 141:167555  
 TITLE: Rapid-onset hypoglycemic effect of **mitiglinide**  
     calcium dihydrate (KAD-1229), a novel  
     antipostprandial-**hyperglycemia** agent.  
     comparison with glimepiride  
 AUTHOR(S): Ojima, Kazuma; Aoyagi, Ikumi; Fujimori, Yoshikazu;  
     Ichikawa, Kiyoshi; Kusama, Hiroshi; Kojima, Masami;  
     Nagasawa, Tatsuya; Ohta, Masanao; Okuhara, Yuji;  
     Kobayashi, Maiko; Tamura, Kei; Kuroda, Junji; Shibata,  
     Nobuo  
 CORPORATE SOURCE: Pharmacology Research Lab. R&D, Kissei Pharmaceutical  
     Co., Ltd., Japan  
 SOURCE: Japanese Pharmacology & Therapeutics (2004), 32(3),  
     161-167  
     CODEN: JPTABU  
 PUBLISHER: Raifu Saiensu Shuppan K.K.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Japanese  
 ED Entered STN: 21 Jun 2004  
 AB The purpose of the present study was to evaluate the hypoglycemic effect of  
     **mitiglinide** calcium dihydrate (KAD-1229), a novel antipostprandial-  
     **hyperglycemia** agent, by comparing it with that of glimepiride, a sulfonylurea  
     agent. In fasted beagle dogs, KAD-1229 (0.15, 0.3 mg/kg) or glimepiride  
     (0.03, 0.06 mg/kg) was administered orally either with no load or just before  
     an oral glucose load. Blood samples were taken from the cephalic vein for the  
     determination of plasma glucose levels. In expts. with no load, plasma  
     insulin levels were also measured. With no glucose load, the hypoglycemic  
     effect of KAD-1229 had a faster onset (at 0.25 h) than that of glimepiride (at  
     1 h), and a shorter duration (0.25-1 h) than that of glimepiride (1-8 h).  
     KAD-1229 stimulated insulin secretion, the peak level occurring within 0.25 h

and a return to baseline within 1 h. In contrast, the peak insulin level occurred at 1 h post-dose in the glimepiride groups. In the oral glucose tolerance test, KAD-1229 rapidly inhibited the increase in plasma glucose (at 0.25 h), and its effect had disappeared within 2 h after its administration. Glimepiride induced a lowering of the plasma glucose level at 1 h after its administration, and at a dose of 0.06 mg/kg, the glucose level given did not return to control values within 8 h. The hypoglycemic effect of KAD-1229 was clearly faster in onset and shorter lasting than that of glimepiride. KAD-1229 can be expected to be more effective than glimepiride at normalizing postprandial hyperglycemia.

CC 1-10 (Pharmacology)

IT Antidiabetic agents

Diabetes mellitus

(rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride)

IT 50-99-7, D-Glucose, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (blood; rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride)

IT 9004-10-8, Insulin, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride)

IT 93479-97-1, Glimepiride 145525-41-3, KAD-1229

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride)

L61 ANSWER 13 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:345396 HCAPLUS Full-text

DOCUMENT NUMBER: 141:325483

TITLE: Rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial hyperglycemic agent: comparison with nateglinide

AUTHOR(S): Ojima, Kazuma; Ichikawa, Kiyoshi; Fujimori, Yoshikazu; Aoyagi, Ikumi; Yamato, Tokuhisa; Tsuji, Atsutoshi; Kusama, Hiroshi; Kojima, Masami; Shibata, Nobuo

CORPORATE SOURCE: Pharmacology Research R & D, Kissei Pharmaceutical Co., Ltd., Japan

SOURCE: Japanese Pharmacology & Therapeutics (2004), 32(2), 73-80

CODEN: JPTABU

PUBLISHER: Raifu Saiensu Shuppan K.K.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 28 Apr 2004

AB Objectives: The purpose of the present study was to evaluate the insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial hyperglycemic agent, by comparison with that of nateglinide. Methods: Mitiglinide calcium dihydrate or nateglinide was administered orally just before an oral-sucrose or liquid-meal load in normal rats, and in mild, moderate, or severe streptozotocin-injected diabetic rats. The plasma insulin and glucose levels were measured. Results: Mitiglinide calcium dihydrate (1 mg/kg) and nateglinide (50 mg/kg) decreased the plasma glucose levels



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significantly at 15-120 min and 15-60 min, resp. in normal rats, and at 30-90 min and 30-60 min, resp., in mildly diabetic rats. These drugs increased the plasma insulin levels at 5-45 min and 5-15 min, resp., in normal rats, and at 15-60 min and 15-45 min, resp., in mildly diabetic rats. In moderately diabetic rats, the antihyperglycemic effects of mitiglinide calcium dihydrate (1 and 3 mg/kg) and nateglinide (50 and 100 mg/kg) were evident at 30-120 min and 30-60 min, resp. In the same rats, mitiglinide, but not nateglinide, significantly increased the plasma insulin levels at 30 min after its administration. Mitiglinide also exhibited antihyperglycemic and insulinotropic effects in the severely diabetic rats. Conclusion: Mitiglinide and nateglinide are suitable drugs for controlling postprandial hyperglycemia. Their antihyperglycemic effects were probably secondary to their rapid-onset, short-lasting insulinotropic effects, and mitiglinide seemed to be a more potent rapid-onset insulinotropic drug than nateglinide.

CC 1-10 (Pharmacology)  
 ST insulinotropic mitiglinide calcium dihydrate KAD1229  
 antipostpradial hyperglycemia nateglinide  
 IT Antidiabetic agents  
 Hyperglycemia  
 (rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostpradial hyperglycemic agent: comparison with nateglinide)  
 IT 105816-04-4, Nateglinide 145525-41-3, KAD-1229  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostpradial hyperglycemic agent: comparison with nateglinide)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 14 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2003:931184 HCAPLUS Full-text  
 DOCUMENT NUMBER: 140:8791  
 TITLE: Therapeutic agent for diabetes  
 INVENTOR(S): Nakanishi, Satoshi; Yano, Hiroshi; Mori, Kiyotoshi; Ogino, Fumiko; Kusaka, Hideaki; Ueno, Kimihisa; Nomoto, Yuji; Matsuda, Yuzuru  
 PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 65 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097064	A1	20031127	WO 2003-JP6136	20030516 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003234929	A1	20031202	AU 2003-234929	20030516 <--

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PRIORITY APPLN. INFO.:

JP 2002-143598

A 20020517 <--

WO 2003-JP6136

W 20030516 <--

OTHER SOURCE(S): MARPAT 140:8791

ED Entered STN: 28 Nov 2003

AB A therapeutic agent for diabetes, is characterized by containing at least one member selected among sulfonylurea antidiabetic agents and sulfonylurea-free K<sup>+</sup> ATP channel blocker antidiabetic agents and at least one member selected among a fused purine derivative and pharmacol. acceptable salts of these. For example, a tablet contained glibenclamide 2, (R)-2-cyclopentyl-7,8-dihydro-8-(4-picolyl)-4-propyl-1H-imidazo[2,1-i]- purin-5(4H)-one d-tartaric acid salt 18, lactose 143.4, starch 30, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg.

IC ICM A61K031-522

ICS A61K031-198; A61K031-4453; A61K031-64; A61K045-00; A61P003-10

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST antidiabetic sulfonylurea potassium channel blocker purine deriv; tablet glibenclamide imidazopurine deriv antidiabetic combination

IT Potassium channel blockers

(ATP-sensitive; antidiabetic combinations for treatment and prevention of diabetes complications and side effects)

IT Sulfonylureas

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antidiabetic combinations for treatment and prevention of diabetes complications and side effects)

IT Drug delivery systems

(capsules; antidiabetic combinations for treatment and prevention of diabetes complications and side effects)

IT Drug delivery systems

(tablets; antidiabetic combinations for treatment and prevention of diabetes complications and side effects)

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide 631-27-6, Glyclopamide 664-95-9, Glycyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1492-02-0, Glybuzol 10238-21-8, Glibenclamide 21187-98-4, Glisclazide 24477-37-0, Glisolamide 25046-79-1, Glisoxepide 26944-48-9, Glibornuride 29094-61-9, Glipizide 32797-92-5, Glisentide 33342-05-1, Gliquidone 93479-97-1, Glimepiride 105816-04-4, Nateglinide 135062-02-1, Repaglinide 145375-43-5, Mitiglinide 254426-47-6 348165-49-1 348362-73-2 349554-62-7 349554-69-4 627512-37-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antidiabetic combinations for treatment and prevention of diabetes complications and side effects)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 15 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:777602 HCAPLUS Full-text

DOCUMENT NUMBER: 139:296975

TITLE: Combination of a HMG-CoA reductase

inhibitor and an insulin secretion enhancer

INVENTOR(S): Damon, Robert Edson; Hughes, Thomas Edward; Burkey, Bryan

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 32 pp.

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CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080070	A2	20031002	WO 2003-EP2978	20030321 <--
WO 2003080070	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2479880	A1	20031002	CA 2003-2479880	20030321 <--
AU 2003209745	A1	20031008	AU 2003-209745	20030321 <--
US 2004002519	A1	20040101	US 2003-393798	20030321 <--
EP 1523316	A2	20050420	EP 2003-744834	20030321 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1642559	A	20050720	CN 2003-806655	20030321 <--
JP 2005526788	T	20050908	JP 2003-577896	20030321 <--
BR 2003008613	A	20050301	BR 2003-8613	20030324 <--
NO 2004004487	A	20041220	NO 2004-4487	20041020 <--
US 2007027197	A1	20070201	US 2006-497130	20060801 <--
PRIORITY APPLN. INFO.:			US 2002-366752P	P 20020322 <--
			US 2003-393798	B1 20030321 <--
			WO 2003-EP2978	W 20030321 <--

ED Entered STN: 03 Oct 2003

AB The present invention relates to a combination pharmaceutical composition comprising as active ingredients (i) a HMG-CoA reductase inhibitor or a salt, (ii) (a) an insulin secretion enhancer or a salt or (b) an insulin sensitizer or a salt. Thus, capsules contained fluvastatin sodium 42.962, CaCO<sub>3</sub> 125.680, NaHCO<sub>3</sub> 4.000, microcryst. cellulose 114.440, pregelatinized starch 83.800, Mg stearate 21.00, and talc 18.860 mg, and water qs.

IC ICM A61K031-64

ICS A61K031-40; A61K031-015; A61K031-435; A61K031-21; A61P005-50; A61K031-404; A61K031-155; A61P003-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST insulin secretion enhancer HMGCoA reductase inhibitor

IT Drug delivery systems

(capsules; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Antiarteriosclerotics

Antidiabetic agents

Antihypertensives

Antiobesity agents

Atherosclerosis

Hypertension

Hypolipemic agents

Hypothyroidism

Kidney, disease

Obesity

(combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Dyslipidemia  
Hyperlipidemia  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Sulfonylureas  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Artery, disease  
(coronary; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Kidney, disease  
(failure; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Liver, disease  
(fatty; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Heart, disease  
(infarction, survival post; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Metabolic disorders  
(metabolic syndrome X; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Diabetes mellitus  
(non-insulin-dependent; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Ovary, disease  
(polycystic; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT Drug delivery systems  
(tablets; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6 657-24-9, Metformin 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybuzole 3149-00-6, Phenbutamide 3459-20-9, Glymidine 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 89750-14-1, GLP-1 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 93957-55-2, Fluvastatin sodium 105816-04-4, Starlix DS 123475-27-4 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 138347-77-0 145375-43-5, Mitiglinide 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 207556-62-5 223607-24-7 274901-16-5 287714-41-4, Rosuvastatin 352513-61-2 355393-49-6 355393-50-9 355393-52-1  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT 9028-35-7, HMG-CoA reductase 54249-88-6, DPP-IV  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(secretion enhancer; combination of HMG-CoA reductase inhibitor and insulin secretion enhancer)

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L61 ANSWER 16 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2003:511859 HCAPLUS Full-text  
 DOCUMENT NUMBER: 139:90459  
 TITLE: Use of an immediate-release powder in pharmaceutical  
 and nutraceutical compositions  
 INVENTOR(S): Besse, Jerome; Besse, Laurence  
 PATENT ASSIGNEE(S): Fr.  
 SOURCE: U.S. Pat. Appl. Publ., 5 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003124191	A1	20030703	US 2002-106923	20020325 <--
FR 2834212	A1	20030704	FR 2001-16934	20011227 <--
FR 2834212	B1	20040709		
CA 2471903	A1	20030710	CA 2002-2471903	20021227 <--
WO 2003055464	A1	20030710	WO 2002-FR4575	20021227 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002364489	A1	20030715	AU 2002-364489	20021227 <--
EP 1458356	A1	20040922	EP 2002-799854	20021227 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002015380	A	20041207	BR 2002-15380	20021227 <--
US 2005118272	A1	20050602	US 2003-500213	20021227 <--
JP 2005520799	T	20050714	JP 2003-556042	20021227 <--
HU 200500509	A2	20050928	HU 2005-509	20021227 <--
NO 2004003172	A	20040914	NO 2004-3172	20040726 <--
PRIORITY APPLN. INFO.:			FR 2001-16934	A 20011227 <--
			WO 2002-FR4575	W 20021227 <--

ED Entered STN: 04 Jul 2003

AB The present invention relates to the use of a powder comprising at least one active substance, at least one surfactant, at least one wetting agent and at least one diluent, for preparing a pharmaceutical or nutraceutical composition, this composition allowing rapid and immediate release of the active substance. Granules containing phloroglucinol 10, sorbitol 89, and propylene glycol 1% were prepared

IC ICM A61K031-7048

ICS A61K031-56; A61K031-522; A61K031-4965; A61K031-445; A61K031-573; A61K031-496; A61K031-4178; A61K031-135

INCL 424489000; 514182000; 514177000; 514178000; 514029000; 514649000; 514317000; 514343000; 514263350; 514554000

CC 63-6 (Pharmaceuticals)

IT Diabetes mellitus

(non-insulin-dependent; use of immediate-release powder in pharmaceutical and nutraceutical compns.)

IT 39391-18-9, Cyclooxygenase

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibitors; use of immediate-release powder in  
pharmaceutical and nutraceutical compns.)

IT 50-03-3, Hydrocortisone acetate 50-23-7, Hydrocortisone 50-28-2,  
Oestradiol, biological studies 50-28-2D, Oestradiol, derivs. 50-70-4,  
Sorbitol, biological studies 50-99-7, Dextrose, biological studies  
51-34-3, Scopolamine 51-98-9, Norethisterone acetate 54-11-5, Nicotine  
54-21-7, Sodium salicylate 55-63-0, Trinitrin 56-81-5, Glycerol,  
biological studies 57-09-0, Cetrimonium bromide 57-13-6, Urea,  
biological studies 57-47-6, Physostigmine 57-48-7, Fructose,  
biological studies 57-50-1, Sucrose, biological studies 57-55-6,  
Propylene glycol, biological studies 57-63-6, Ethinyl oestradiol  
57-83-0, Progesterone, biological studies 58-08-2, Caffeine, biological  
studies 58-22-0, Testosterone 59-66-5, Acetazolamide 60-40-2,  
Mecamylamine 63-42-3, Lactose 64-17-5, Ethanol, biological studies  
67-73-2, Fluocinolone acetonide 69-65-8, Mannitol 71-52-3,  
Bicarbonate, biological studies 81-13-0, Dexpanthenol 87-33-2,  
Isosorbide dinitrate 87-99-0, Xylitol 89-78-1, Menthol 94-36-0,  
Benzoyl peroxide, biological studies 97-53-0, Eugenol 101-20-2,  
Triclocarban 106-24-1, Geraniol 106-25-2, Nerol 106-60-5,  
5-Aminolevulinic acid 108-73-6, Phloroglucinol 110-27-0, Isopropyl  
myristate 112-62-9, Methyl oleate 112-80-1, Oleic acid, biological  
studies 113-45-1, Methyl phenidate 114-07-8, Erythromycin 123-03-5,  
Cetylpyridinium chloride 124-94-7, Triamcinolone 137-58-6, Lidocaine  
139-33-3 143-07-7, Lauric acid, biological studies 144-80-9,  
Sulphacetamide 145-42-6, Sodium taurocholate 147-24-0, Diphenhydramine  
hydrochloride 151-21-3, Sodium lauryl sulphate, biological studies  
152-97-6, Fluocortolone 302-79-4, Tretinoin 303-40-2, Fluocortolone  
hexanoate 356-12-7, Fluocinolide 437-38-7, Fentanyl 443-48-1,  
Metronidazole 470-82-6, Eucalyptol 471-34-1, Calcium carbonate,  
biological studies 497-19-8, Sodium carbonate, biological studies  
521-18-6, Dihydrotestosterone 585-86-4, Lactitol 611-53-0, Ibacitabine  
638-94-8, Desonide 645-92-1 745-65-3, Alprostadil 797-63-7,  
Levonorgestrel 863-57-0, Sodium glycocholate 1180-95-6, Sodium  
taurodeoxycholate 2002-29-1, Flumetasone pivalate 2152-44-5,  
Betamethasone valerate 2438-72-4, Bufexamac 3764-87-2 4205-90-7,  
Clonidine 4394-00-7, Niflumonic acid 4759-48-2, Isotretinoin  
4985-25-5, Pyrazinobutazone 5104-49-4, Flurbiprofen 5593-20-4,  
Betamethasone dipropionate 5633-20-5, Oxybutynin 5716-20-1, Bamethan  
sulfate 6805-41-0, Escin 7757-93-9, Dibasic calcium phosphate  
7758-87-4, Tribasic calcium phosphate 7759-35-5, Nestorone 7778-18-9,  
Calcium sulphate 9000-30-0, Guar gum 9002-72-6, Growth hormone  
9003-39-8, Povidone 9004-10-8, Insulin, biological studies 9004-32-4,  
Sodium carboxymethylcellulose 9004-53-9, Dextrins 9004-57-3,  
Ethylcellulose 9004-65-3, Hydroxypropylmethylcellulose 9004-67-5,  
Methylcellulose 9005-25-8, Starch, biological studies 9005-32-7,  
Alginic acid 9005-63-4D, Polyoxyethylene sorbitan, esters with fatty  
acids 9005-65-6, Polysorbate 80 9042-14-2, Dextran sulphate  
9087-70-1, Aprotinin 12619-70-4, Cyclodextrins 12794-10-4,  
Benzodiazepine 14611-51-9, Selegiline 15307-86-5, Diclofenac  
15687-27-1, Ibuprofen 16409-34-0, Sodium glycodeoxycholate 18559-94-9,  
Salbutamol 19216-56-9, Prazosin 22071-15-4, Ketoprofen 22832-87-7,  
Miconazole nitrate 22916-47-8, Miconazole 23674-86-4, Difluprednate  
24169-02-6, Econazole nitrate 25122-46-7, Clobetasol propionate  
25322-68-3, Polyethylene glycol 25655-41-8, Povidone Iodine  
25717-80-0, Molsidomine 28981-97-7, Alprozolam 29205-06-9,  
Fluocortolone pivalate 29679-58-1, Fenoprofen 29984-33-6, Vidarabine  
monophosphate 34580-13-7, Ketotifen 36322-90-4, Piroxicam  
36505-84-7, Buspirone 38304-91-5, Minoxidil 39219-28-8, Promestriene  
39404-33-6, Dextrates 39809-25-1, Penciclovir 41570-61-0, Tulobuterol  
51022-69-6, Amcinonide 52485-79-7, Buprenorphine 53016-31-2,

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Norelgestromin 59198-70-8, Diflucortolone Valerate 59227-89-3, Azone 59277-89-3, Acyclovir 60282-87-3, Gestodene 65277-42-1, Ketoconazole 66104-22-1, Pergolide 66734-13-2, Alclometasone dipropionate 72522-13-5, Eptazocine 74103-06-3, Ketorolac 80214-83-1, Roxithromycin 99011-02-6, Imiquimod 99755-59-6, Rotigotine 106685-40-9, Adapalene 113775-47-6, Dexmedetomidine 118292-40-3, Tazarotene 119141-88-7, Esomeprazole 122852-42-0, Alosetron 129722-12-9, Aripiprazole 133099-04-4, Darifenacin 137234-62-9, Voriconazole 141563-69-1, OrZel 143322-58-1, Eletriptan 145158-71-0, Tegaserod 145209-50-3, Thiatolserine 145375-43-5, Mitiglinide 147511-69-1, Pitavastatin 147657-22-5, Calcipotriol monohydrate 153259-65-5, Cilomilast 154189-24-9, Viozan 159776-70-2, Melagatran 163222-33-1 167305-00-2, Omapatrilat 178979-85-6, Capravirine 179463-17-3, Caspofungin acetate 181695-72-7, Valdecixib 198470-84-7, Parecoxib 202409-33-4, Etoricoxib 287714-41-4, Rosuvastatin 552881-25-1, Crilanomer

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(use of immediate-release powder in pharmaceutical and nutraceutical compns.)

L61 ANSWER 17 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:473243 HCAPLUS Full-text

DOCUMENT NUMBER: 139:41849

TITLE: Pharmaceutical compositions containing a renin inhibitor and antidiabetics

INVENTOR(S): Webb, Randy Lee

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 7 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003114389	A1	20030619	US 2002-290651	20021108 <--
US 2005101638	A1	20050512	US 2004-14141	20041216 <--
US 2007093431	A1	20070426	US 2006-614401	20061221 <--
PRIORITY APPLN. INFO.:			US 2001-350708P	P 20011113 <--
			US 2002-290651	B1 20021108 <--
			US 2004-14141	A1 20041216

ED Entered STN: 20 Jun 2003

AB The invention relates to a composition comprising a renin inhibitor (e.g., aliskiren) or a salt thereof and at least 1 antidiabetic agent. Thus, a hemifumarate of aliskiren 1000, corn starch 680, colloidal silica 200, Mg stearate 20, stearic acid 50, sodium carboxymethyl starch 250, and water qs to 1000 g.

IC ICM A61K038-04

ICS A61K031-4439; A61K031-426; A61K031-175; A61K031-16

INCL 514019000; 514342000; 514369000; 514592000; 514629000

CC 63-6 (Pharmaceuticals)

ST pharmaceutical antidiabetic renin inhibitor; aliskiren renin inhibitor pharmaceutical

IT Antidiabetic agents

Diabetes mellitus

Drug delivery systems

(pharmaceutical compns. containing renin inhibitor and antidiabetics)

IT Sulfonylureas

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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical compns. containing renin inhibitor and  
antidiabetics)

IT Drug delivery systems  
(tablets, coated; pharmaceutical compns. containing renin inhibitor  
and antidiabetics)

IT Drug delivery systems  
(tablets; pharmaceutical compns. containing renin inhibitor and  
antidiabetics)

IT 9015-94-5, Renin, biological studies 54249-88-6, DPP-IV  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor; pharmaceutical compns. containing renin  
inhibitor and antidiabetics)

IT 89750-14-1, GLP1  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(pharmaceutical compns. containing renin inhibitor and  
antidiabetics)

IT 657-24-9, Metformin 105816-04-4, Nateglinide 111025-46-8, Pioglitazone  
122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 145375-43-5  
, Mitiglinide 173334-57-1, Aliskiren 173334-58-2  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical compns. containing renin inhibitor and  
antidiabetics)

IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(secretion enhancer; pharmaceutical compns. containing renin  
inhibitor and antidiabetics)

L61 ANSWER 18 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:293592 HCAPLUS Full-text

DOCUMENT NUMBER: 136:325420

TITLE: Drugs for diabetes, especially type 2,  
comprising an antiinflammatory or analgesic drug,  
selected bivalent linkers, and a nitrate ester

INVENTOR(S): Del Soldato, Piero

PATENT ASSIGNEE(S): Nicox S.A., Fr.

SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

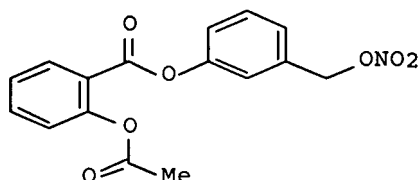
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 2002030867	A2	20020418	WO 2001-EP11665	20011009 <--
WO 2002030867	A3	20020725		
W:	AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
IT 2000MI2201	A1	20020412	IT 2000-MI2201	20001012 <--
IT 1319201	B1	20030926		
CA 2425655	A1	20020418	CA 2001-2425655	20011009 <--
AU 200214006	A	20020422	AU 2002-14006	20011009 <--
EP 1324974	A2	20030709	EP 2001-982414	20011009 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			



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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 JP 2004511456 T 20040415 JP 2002-534256 20011009 <--  
 US 2004023890 A1 20040205 US 2003-398511 20030411 <--  
 PRIORITY APPLN. INFO.: IT 2000-MI2201 A 20001012 <--  
 WO 2001-EP11665 W 20011009 <--  
 OTHER SOURCE(S): MARPAT 136:325420  
 ED Entered STN: 19 Apr 2002  
 GI



II

- AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)n-(C)m-NO<sub>2</sub> [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies, neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of . desoxyribose in aqueous Fe<sup>2+</sup>/(NH<sub>4</sub>)<sub>2</sub>(SO<sub>4</sub>)<sub>2</sub>/thiobarbituric acid solution; and (test 4): inhibition by ≥ 50% of DPPH-induced radical production in MeOH solution. For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitration of the resultant Ph ester with HNO<sub>3</sub>/H<sub>2</sub>SO<sub>4</sub> (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10<sup>-4</sup> M gave 70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.
- IC ICM C07C203-04  
 ICS A61K031-04; A61K031-621; A61P003-10
- CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
 Section cross-reference(s): 1
- IT Diabetes mellitus  
 (non-insulin-dependent, treatment; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)
- IT 50-81-7, Ascorbic acid, properties 52-67-5, Penicillamine 52-90-4, Cysteine, properties 56-69-9, 5-Hydroxytryptophan 56-84-8, Aspartic acid, properties 57-50-1, Saccharose, properties 60-00-4, Edetic acid, properties 60-24-2, 2-Mercaptoethanol 70-18-8, Glutathione, properties

71-00-1, Histidine, properties 77-92-9, Citric acid, properties  
 80-72-8, Reductic acid 89-65-6, Isoascorbic acid 105-59-9,  
 N-Methyldiethanolamine 110-15-6, Succinic acid, properties 110-17-8,  
 Fumaric acid, properties 110-63-4, 1,4-Butanediol, properties  
 111-17-1, 3,3'-Thiodipropionic acid 111-46-6, Diethylene glycol,  
 properties 111-48-8, Thiodiethylene glycol 117-39-5, Quercetin  
 120-05-8, Sulfuretin 121-34-6, Vanillic acid 121-79-9, Propyl gallate  
 123-31-9, Hydroquinone, properties 141-90-2, 2-Thiouracil 149-91-7,  
 Gallic acid, properties 154-23-4, Catechin 303-45-7, Gossypol  
 305-84-0, L-Carnosine 331-39-5, Caffeic acid 444-27-9,  
 4-Thiazolidinecarboxylic acid 458-35-5, Coniferyl alcohol 490-79-9,  
 Gentisic acid 500-38-9, Nordihydroguaiaretic acid 501-94-0 520-18-3,  
 Kaempferol 520-26-3, Hesperidin 526-84-1, Dihydroxymaleic acid  
 533-73-3, Hydroxyhydroquinone 584-85-0, Anserine 591-81-1,  
 4-Hydroxybutyric acid 635-65-4, Bilirubin, properties 824-46-4,  
 Methoxyhydroquinone 1005-72-7, Tetrahydropyran-2,6-dimethanol  
 1077-28-7, Thioctic acid 1191-25-9, 6-Hydroxyhexanoic acid 1406-18-4,  
 Vitamin E 1464-42-2, Selenomethionine 3614-08-2, Selenocysteine  
 3690-05-9, p-Cumaric alcohol 6007-86-9, Thiophene-2,5-dimethanol  
 7400-08-0, p-Cumaric acid 15537-71-0, N-Acetylpenicillamine  
 19750-45-9, 2-Oxo-4-thiazolidinecarboxylic acid 54120-69-3,  
 1,4-Dioxan-2,6-dimethanol 54573-75-0, 1 $\alpha$ -OH-Vitamin D2  
 55721-11-4, Secalciferol 63147-28-4, 3,5-Di-tert-butyl-4-hydroxybenzyl  
 thioglycolate 83805-11-2, Flocalcitriol 92614-59-0, Glutathione ethyl  
 ester 97451-46-2, Glutathione isopropyl ester 103909-75-7,  
 22-Oxacalcitriol 148258-92-8 326850-58-2, Tetrahydrothiopyran-2,6-  
 dimethanol 326850-59-3, 1,4-Dithiane-2,6-dimethanol 326850-60-6,  
 Cyclohexene-1,5-dimethanol 326850-61-7, Thiazole-2,5-dimethanol  
 326850-62-8, Oxazole-2,5-dimethanol 414355-30-9, 4H-Pyran-2,6-dimethanol  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)

(bivalent linker precursor; preparation of antidiabetic agents comprising  
 antiinflammatory or analgesic drugs, selected bivalent linkers, and  
 nitrate esters)

IT 50-78-2DP, Acetylsalicylic acid, nitroxyl-containing derivs. 61-68-7DP,  
 Mefenamic acid, nitroxyl-containing derivs. 65-45-2DP, Salicylamide,  
 nitroxyl-containing derivs. 69-72-7DP, Salicylic acid, nitroxyl-containing  
 derivs. 89-45-2DP, Salicylsulfuric acid, nitroxyl-containing derivs.  
 118-55-8DP, Phenyl salicylate, nitroxyl-containing derivs. 118-57-0DP,  
 Acetaminosalol, nitroxyl-containing derivs. 487-48-9DP, Salacetamide,  
 nitroxyl-containing derivs. 530-75-6DP, Acetylsalicylsalicylic acid,  
 nitroxyl-containing derivs. 530-78-9DP, Flufenamic acid, nitroxyl-containing  
 derivs. 552-94-3DP, Salsalate, nitroxyl-containing derivs. 644-62-2DP,  
 Meclofenamic acid, nitroxyl-containing derivs. 695-34-1DP,  
 2-Amino-4-picoline, nitroxyl-containing derivs. 1503-53-3DP,  
 5-Bromosalicylic acid acetate, nitroxyl-containing derivs. 4394-00-7DP,  
 Niflumic acid, nitroxyl-containing derivs. 5104-49-4DP, Flurbiprofen,  
 nitroxyl-containing derivs. 13710-19-5DP, Tolfenamic acid, nitroxyl-  
 containing  
 derivs. 15687-27-1DP, Ibuprofen, nitroxyl-containing derivs. 38194-50-2DP,  
 Sulindac, nitroxyl-containing derivs. 38677-85-9DP, Flunixin,  
 nitroxyl-containing derivs. 87893-55-8DP, 15-Deoxy- $\Delta^{12,14}$ -  
 prostaglandin, nitroxyl-containing derivs. 105816-04-4DP, Nateglinide,  
 nitroxyl-containing derivs. 135062-02-1DP, Repaglinide, nitroxyl-containing  
 derivs. 145375-43-5DP, Mitiglinide, nitroxyl-containing  
 derivs. 177785-17-0DP, (S)-4-[2-(2-Benzoxazolylmethylamino)ethoxy]-  
 $\alpha$ -(2,2,2-trifluoroethoxy)benzenepropanoic acid, nitroxyl-containing  
 derivs. 195137-72-5DP, JTT-608, nitroxyl-containing derivs. 196808-24-9DP,  
 N-(2-Benzoylphenyl)-O-[2-(methyl-2-pyridinylamino)ethyl]-L-tyrosine,

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nitroxyl-containing derivs. 196808-45-4DP, Farglitazar, nitroxyl-containing derivs. 236111-01-6DP, (S)-4-[2-(2-Benzoxazolylmethylamino)ethoxy]- $\alpha$ -ethoxybenzenepropanoic acid, nitroxyl-containing derivs. 267412-60-2DP, (2S,5S)-N,N-Dibenzyl-3-[4-(4-Carboxyphenyl)butyl]-2-heptyl-4-oxothiazolidine-5-acetamide, nitroxyl-containing derivs. 403731-62-4DP, Rosiglitazone nitrate, nitroxyl-containing derivs. 414355-31-0DP, Pioglitazone nitrate, nitroxyl-containing derivs.  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidates; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

L61 ANSWER 19 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:157602 HCAPLUS Full-text

DOCUMENT NUMBER: 136:205430

TITLE: Pharmaceutical compositions containing AT-receptor antagonist or insulin secretion enhancers

INVENTOR(S): Allison, Malcolm; Gatlin, Marjorie Regan

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Novartis Pharma. GmbH

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015933	A2	20020228	WO 2001-EP9587	20010820
WO 2002015933	A3	20030814		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2001087698	A5	20020304	AU 2001-87698	20010820
EP 1351683	A2	20031015	EP 2001-967289	20010820
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004514654	T	20040520	JP 2002-520854	20010820
US 2004034065	A1	20040219	US 2003-362340	20030616
US 2006089389	A1	20060427	US 2005-295928	20051207
US 2006281790	A1	20061214	US 2006-508353	20060823
PRIORITY APPLN. INFO.:			US 2000-643641	A 20000822
			US 2000-327553P	P 20000822
			WO 2001-EP9587	W 20010820
			US 2003-362340	B1 20030616
			US 2005-295928	B1 20051207

ED Entered STN: 01 Mar 2002

AB A pharmaceutical composition comprises as active ingredients an AT1-receptor antagonist or a salt, an insulin secretion enhancer or a its salt or an insulin sensitizer or its salt. Thus, tablets contained Starlix DS 60,

lactose monohydrate 141.5, microcryst. cellulose 71, Povidone-K30 12, and Croscarmellose sodium 18.4, colloidal SiO<sub>2</sub> 6.4, Mg stearate 5.7, and Opadry 9 mg.

IC ICM A61K045-00  
 CC 63-6 (Pharmaceuticals)  
 IT Angiotensin receptor antagonists  
 Antianginal agents  
 Antidiabetic agents  
 Antihypertensives  
 Antiobesity agents  
 Cardiovascular agents  
 Cataract  
 Connective tissue, disease  
     **Hyperglycemia**  
 Hypertriglyceridemia  
 Hypolipemic agents  
 Skin, disease  
     (pharmaceutical compns. containing AT-receptor antagonist or insulin secretion enhancers)  
 IT 339-43-5, Carbutamide 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6, Glyclopamide 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybuzole 3149-00-6, Phenbutamide 3459-20-9, Glymidine 4618-41-1, 1-Butyl-3-metanilylurea 9004-10-8, Insulin, biological studies 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 93479-97-1, Glimepiride 105816-04-4, Nateglinide 114798-26-4, Losartan 133040-01-4, Eprosartan 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 139481-59-7, Candesartan 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan 145375-43-5, Mitiglinide 145733-36-4, Tasosartan  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (pharmaceutical compns. containing AT-receptor antagonist or insulin secretion enhancers)

L61 ANSWER 20 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2002:157564 HCAPLUS Full-text  
 DOCUMENT NUMBER: 136:205424  
 TITLE: Combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors  
 INVENTOR(S): Allison, Malcolm; Gatlin, Marjorie Regan  
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Novartis Pharma GmbH  
 SOURCE: PCT Int. Appl., 21 pp.  
           CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015892	A2	20020228	WO 2001-EP9586	20010820 <--
WO 2002015892	A3	20030904		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,				

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PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,  
US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,  
KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,  
IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002014952 A5 20020304 AU 2002-14952 20010820 <--

EP 1359907 A2 20031112 EP 2001-983442 20010820 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004519424 T 20040702 JP 2002-520813 20010820 <--

US 2004087630 A1 20040506 US 2003-362341 20030618 <--

PRIORITY APPLN. INFO.: US 2000-643642 A 20000822 <--

WO 2001-EP9586 W 20010820 <--

ED Entered STN: 01 Mar 2002

AB The present invention relates to a combination, especially a pharmaceutical composition, comprising (a) an insulin secretion enhancer or a pharmaceutically acceptable salt thereof and (b) at least one of the active ingredients selected from the group consisting of (i) HMG-Co-A reductase inhibitors or a pharmaceutically acceptable salt thereof; and (ii) ACE inhibitors or a pharmaceutically acceptable salt thereof; and, in case of a pharmaceutical composition, a pharmaceutically acceptable carrier. Formulations were given as examples, e.g., tablets containing nateglinide.

IC ICM A61K031-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST insulin secretion enhancer pharmaceutical combination; HMG CoA reductase inhibitor pharmaceutical combination; acetylcholinesterase inhibitor pharmaceutical combination

IT Antidiabetic agents

Antihypertensives

Antiobesity agents

Connective tissue, disease

Eye, disease

Hypolipemic agents

Skin, disease

(combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Nerve, disease

(diabetic neuropathy; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Eye, disease

(diabetic retinopathy; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Heart, disease

(failure; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Kidney, disease

(glomerulosclerosis; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Sexual disorders

(impotence; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Eye, disease

(macula, degeneration; combinations of insulin secretion enhancer,

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HMG-CoA reductase inhibitors and  
acetylcholinesterase inhibitors)

- IT Inflammation  
Intestine, disease  
(ulcerative colitis; combinations of insulin secretion enhancer,  
HMG-CoA reductase inhibitors and  
acetylcholinesterase inhibitors)
- IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(combinations of insulin secretion enhancer, HMG-CoA reductase  
inhibitors and acetylcholinesterase inhibitors)
- IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide  
339-44-6, Glymidine 451-71-8, Glyhexamide 535-65-9, Glybuthiazole  
631-27-6, Glyclopamide 664-95-9, Tolcyclamide 968-81-0,  
Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide  
1492-02-0, Glybuzole 3149-00-6, Phenbutamide 4618-41-1,  
1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 21187-98-4,  
Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride  
29094-61-9, Glipizide 33342-05-1, Gliquidone 62571-86-2, Captopril  
74258-86-9, Alacepril 75330-75-5, Lovastatin 75847-73-3, Enalapril  
76420-72-9, Enalaprilat 76547-98-3, Lisinopril 79902-63-9, Simvastatin  
81093-37-0, Pravastatin 82834-16-0, Perindopril 83435-66-9, Delapril  
83647-97-6, Spirapril 85441-61-8, Quinapril 85856-54-8, Moveltipril  
86541-75-5, Benazepril 86541-78-8, Benazeprilat 87333-19-5, Ramipril  
87679-37-6, Trandolapril 88768-40-5, Cilazapril 89371-37-9, Imidapril  
93479-97-1, Glimepiride 93957-54-1, Fluvastatin 98048-97-6, Fosinopril  
105816-04-4, Nateglinide 111223-26-8, Ceronapril 111902-57-9,  
Temocapril 134523-00-5, Atorvastatin 135062-02-1, Repaglinide  
145375-43-5, Mitiglinide 145599-86-6, Cerivastatin  
147511-69-1, Pitavastatin 287714-41-4, Rosuvastatin  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combinations of insulin secretion enhancer, HMG-CoA reductase  
inhibitors and acetylcholinesterase inhibitors)
- IT 9000-81-1, Acetylcholinesterase 9028-35-7, HMG-CoA reductase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; combinations of insulin secretion enhancer,  
HMG-CoA reductase inhibitors and  
acetylcholinesterase inhibitors)

L61 ANSWER 21 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:51257 HCAPLUS Full-text

DOCUMENT NUMBER: 136:123595

TITLE: A combination of phosphonate or phosphorodiamidate  
FBPase inhibitors and antidiabetic agents  
useful for the treatment of diabetes

INVENTOR(S): Van Poelje, Paul D.; Erion, Mark D.; Fujiwara,  
Toshihiko

PATENT ASSIGNEE(S): Metabasis Therapeutics, Inc., USA; Sankyo Company,  
Ltd.

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WO 2002003978	A3	20031016		

10/519155

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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IN 2002MN01873	A	20050204	IN 2002-MN1873	20021224 <--
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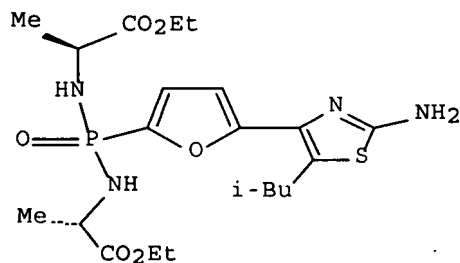
PRIORITY APPLN. INFO.:

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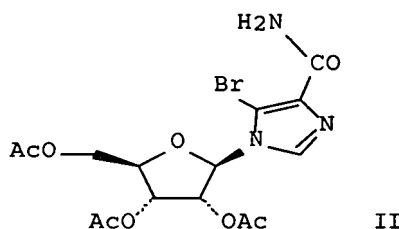
OTHER SOURCE(S): MARPAT 136:123595

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GI



I



II

AB A combination therapy of at least one FBPase inhibitor ((R1Y)2P(O)M and R14C(O) (CR12R13)nN(R18)P(O) (NR15R16)M; e.g. 2-amino-5-propylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide and 2-amino-5-isobutyl-4-[2-[N,N'-bis[(S)-1-(ethoxycarbonyl)ethyl]phosphonodiamido]-5-furanyl]thiazole (shown as I)) and at least one other antidiabetic agent (insulin secretagogue; e.g. glyburide, a sulfonylurea) is disclosed. (R1Y)2P(O)M and R14C(O) (CR12R13)nN(R18)P(O) (NR15R16)M are converted in vivo or in vitro to MPO32-, which inhibit FBPase; the substituents are defined in the claims. General methods and about 15 specific example prepns. of the phosphorus

compds. are included but no methods of preparation are claimed. In the biol. examples, data is presented for the following for selected phosphorus compds. and other materials: inhibition of human liver FBPase, inhibition of rat liver and mouse liver FBPase, inhibition of gluconeogenesis by an FBPase inhibitor in rat hepatocytes, inhibition of glucose production and elevation of fructose-1,6-bisphosphate levels in rat hepatocytes treated with FBPase inhibitors, anal. of hepatic and plasma drug metabolite levels, blood glucose, and hepatic fructose 1,6-bisphosphate levels after administration of compound A (shown as II) p.o. to normal fasted rats, anal. of hepatic and plasma drug levels after administration of compds. i.p. to normal fasted rats, oral bioavailability determination of two compds. and oral glucose lowering activity of two compds. For insulin secretagogues: insulin release from pancreatic islets, glucose lowering in the fasted rat, i.v. glucose tolerance in the fasted rat, oral glucose tolerance in the Zucker diabetic fatty rat, insulin secretion in the rat, inhibition of KATP-channels in mouse pancreatic beta-cells, and sulfonylurea receptor binding. Also included are: inhibition of dipeptidyl peptidase IV (DPP-IV inhibitors), alpha-glucosidase assay, glycogen phosphorylase assay, assay of glucose 6-phosphatase inhibitors, glucagon antagonist assay, amylin agonist assay, fatty acid oxidation inhibitor assay, glucose lowering in the db/db mouse (FBPase inhibitor), glucose lowering in the ZDF rat, acute combination treatment of an insulin secretagogue and an FBPase inhibitor in the ZDF rat, chronic combination treatment of an insulin secretagogue and an FBPase inhibitor in the ZDF rat, acute combination treatment of insulin and an FBPase inhibitor in db/db mice, beneficial effect of chronic combination treatment of insulin and an FBPase inhibitor in db/db mice, and beneficial effect of chronic combination treatment of insulin and an FBPase inhibitor in db/db Mice. Also included are: acute combination treatment of insulin and an FBPase inhibitor in the Goto-Kakizaki rat, acute combination treatment of a biguanide and an FBPase inhibitor in db/db mice, acute combination treatment of an alpha glucosidase inhibitor and an FBPase inhibitor in Goto-Kakizaki rats, acute combination treatment of a glycogen phosphorylase inhibitor and an FBPase inhibitor in db/db or ob/ob mice, acute combination treatment of a glucose-6-phosphatase inhibitor and an FBPase inhibitor in db/db or ob/ob mice, acute combination treatment of an FBPase inhibitor and an amylin agonist, chronic combination treatment of a fatty acid oxidation inhibitor and an FBPase inhibitor in the streptozotocin-induced diabetic rat.

IC ICM A61K031-00

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1, 27, 28, 29

ST antidiabetic agent phosphonate phosphorodiamidate FBPase inhibitor  
diabetes treatment; insulin secretagogue phosphonate  
phosphorodiamidate FBPase inhibitor diabetes treatment

IT Potassium channel

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(ATP-sensitive; combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)

IT Glucagon-like peptide-1 receptors

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(agonists; combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)

IT Sulfonylurea receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(binding; combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)

IT Antiobesity agents



(combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful as)

- IT Antidiabetic agents
  - B cell (lymphocyte)
  - Drug bioavailability
  - Human
  - Pancreatic islet of Langerhans
    - (combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)
- IT Antioxidants
  - (fatty acid; combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)
- IT Liver
  - (fructose biphosphatase of; combination of phosphonate or  
phosphorodiamidate FBPase inhibitors and antidiabetic agents  
useful for treatment of diabetes)
- IT Liver
  - (hepatocyte, fructose biphosphatase of; combination of phosphonate or  
phosphorodiamidate FBPase inhibitors and antidiabetic agents  
useful for treatment of diabetes)
- IT Gluconeogenesis
  - (inhibitors; combination of phosphonate or phosphorodiamidate  
FBPase inhibitors and antidiabetic agents useful for  
treatment of diabetes)
- IT Fatty acids, biological studies
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; combination of phosphonate or phosphorodiamidate  
FBPase inhibitors and antidiabetic agents useful for  
treatment of diabetes)
- IT Sulfonylureas
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(insulin secretagogues; combination of phosphonate or  
phosphorodiamidate FBPase inhibitors and antidiabetic agents  
useful for treatment of diabetes)
- IT Drug delivery systems
  - (oral; combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)
- IT Organic compounds, biological studies
  - RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)  
(phosphorus-containing; combination of phosphonate or phosphorodiamidate  
FBPase inhibitors and antidiabetic agents useful for  
treatment of diabetes)
- IT Drug delivery systems
  - (prodrugs; combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)
- IT 106602-62-4, Amylin
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(agonists; combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)
- IT 151126-32-8, Pramlintide
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(amylin agonist; combination of phosphonate or phosphorodiamidate  
FBPase inhibitors and antidiabetic agents useful for  
treatment of diabetes)

- IT 9007-92-5, Glucagon, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(antagonists; combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)
- IT 50-99-7, D-Glucose, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(blood; combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)
- IT 213125-12-3P, 5-Diethylphosphono-2-(4-methyl-1-oxopentyl)furan  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); RACT (Reactant or reagent); USES (Uses)  
(combination of phosphonate or phosphorodiamidate FBPase  
inhibitors and antidiabetic agents useful for treatment of  
diabetes)
- IT 261365-06-4P, 5-Diethylphosphono-2-acetylfuran 261365-08-6P,  
5-Diethylphosphono-2-(1-oxobutyl)furan 261365-11-1P,  
2-Amino-5-isobutyl-4-[5-phosphono-2-furanyl]thiazole 261365-17-7P  
261365-19-9P, 2-Methyl-4-(5-phosphono-2-furanyl)thiazole 261365-23-5P,  
2-Isopropyl-4-(5-phosphono-2-furanyl)thiazole 261365-25-7P,  
5-Isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-27-9P,  
2-Aminothiocabonyl-4-(5-phosphono-2-furanyl)thiazole 261365-31-5P  
261365-33-7P, 2-(2-Thienyl)-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole  
261365-36-0P 261365-37-1P, 2-Acetamido-5-isobutyl-4-(5-phosphono-2-  
furanyl)thiazole 261365-38-2P, 2-Amino-4-(5-phosphono-2-furanyl)thiazole  
261365-40-6P, 2-Methylamino-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole  
261365-44-0P 261365-48-4P 261365-51-9P 261365-55-3P 261365-56-4P,  
2-Ethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-58-6P,  
2-Amino-5-ethyl-4-(5-phosphono-2-furanyl)thiazole 261365-60-0P,  
2-Cyanomethyl-4-(5-phosphono-2-furanyl)thiazole 261365-62-2P  
261365-63-3P, 2-Amino-5-propyl-4-(5-phosphono-2-furanyl)thiazole  
261365-65-5P 261365-66-6P, 2-Amino-5-methylthio-4-(5-phosphono-2-  
furanyl)thiazole 261365-67-7P, 2-Amino-5-cyclopropyl-4-(5-phosphono-2-  
furanyl)thiazole monohydrobromide 261365-68-8P, 2-Amino-5-cyclopropyl-4-  
(5-phosphono-2-furanyl)thiazole 261365-70-2P, 2-Amino-5-  
benzyloxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-72-4P  
261365-73-5P, 2-Amino-5-[N,N-dimethylaminomethyl]-4-(5-phosphono-2-  
furanyl)thiazole dihydrobromide 261365-75-7P, 2-Amino-5-methoxycarbonyl-  
4-(5-phosphono-2-furanyl)thiazole 261365-78-0P, 2-Amino-5-  
propyloxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-79-1P,  
2-Amino-5-benzyl-4-(5-phosphono-2-furanyl)thiazole 261365-80-4P,  
2-Amino-5-[N,N-diethylaminomethyl]-4-(5-phosphono-2-furanyl)thiazole  
dihydrobromide 261365-83-7P, 2-Amino-5-(N,N-dimethylcarbamoyl)-4-(5-  
phosphono-2-furanyl)thiazole 261365-85-9P, 2-Amino-5-carboxy-4-(5-  
phosphono-2-furanyl)thiazole 261365-86-0P, 2-Amino-5-  
isopropylloxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-89-3P,  
2-Methyl-5-cyclopropyl-4-(5-phosphono-2-furanyl)thiazole 261365-90-6P,  
2-Methyl-5-ethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole  
261365-92-8P, 2-[N-Acetylmino]-5-methoxymethyl-4-(5-phosphono-2-  
furanyl)thiazole 261365-95-1P, 2-Amino-5-cyclopropylmethoxycarbonyl-4-(5-  
phosphono-2-furanyl)thiazole 261365-98-4P, 2-[(N-Dansyl)amino]-5-  
isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-99-5P,  
2-Amino-5-(2,2,2-trifluoroethyl)-4-(5-phosphono-2-furanyl)thiazole  
261366-00-1P, 2-Methyl-5-methylthio-4-(5-phosphono-2-furanyl)thiazole  
261366-01-2P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)thiazole

monoammonium salt 261366-02-3P, 2-Cyano-5-ethyl-4-(5-phosphono-2-furanyl)thiazole 261366-03-4P, 2-Amino-5-hydroxymethyl-4-(5-phosphono-2-furanyl)thiazole 261366-05-6P, 2-Cyano-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261366-06-7P, 2-Amino-5-isopropylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide 261366-07-8P, 2-Amino-5-phenylthio-4-(5-phosphono-2-furanyl)thiazole 261366-08-9P, 2-Amino-5-tert-butylthio-4-(5-phosphono-2-furanyl)thiazole 261366-09-0P, 2-Amino-5-propylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide 261366-11-4P, 2-Amino-5-ethylthio-4-(5-phosphono-2-furanyl)thiazole 261366-12-5P, 2-[N-(tert-Butyloxycarbonyl)amino]-5-methoxymethyl-4-(5-phosphono-2-furanyl)thiazole 261366-13-6P, 2-Hydroxy-4-(5-phosphono-2-furanyl)thiazole 261366-14-7P, 2-Hydroxy-5-ethyl-4-(5-phosphono-2-furanyl)thiazole 261366-16-9P, 2-Hydroxy-5-isopropyl-4-(5-phosphono-2-furanyl)thiazole 261366-17-0P, 2-Hydroxy-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261366-18-1P, 5-Ethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261366-20-5P, 2-Amino-5-vinyl-4-(5-phosphono-2-furanyl)thiazole 261366-21-6P, 2-Methylthio-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261366-24-9P, 2-Amino-5-isobutyl-4-(5-phosphono-2-furanyl)selenazole 261366-26-1P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)selenazole 261366-40-9P, 2-Amino-5-(2-furanyl)-4-(5-phosphono-2-furanyl)thiazole 261366-65-8P, 2-Amino-5-isobutyl-4-(5-phosphono-2-furanyl)oxazole 261366-66-9P, 2-Hydroxy-5-isobutyl-4-(5-phosphono-2-furanyl)imidazole 261366-67-0P, 2-Methyl-4-isobutyl-5-(5-phosphono-2-furanyl)oxazole monohydrobromide 261366-68-1P, 2-Methyl-5-isobutyl-4-(5-phosphono-2-furanyl)oxazole monohydrobromide 261366-69-2P, 2-Methyl-5-isobutyl-4-(5-phosphono-2-furanyl)imidazole monohydrobromide 261366-71-6P, 2-Trifluoromethyl-4-(5-phosphono-2-furanyl)imidazole 261366-73-8P, 4,5-Dimethyl-1-isobutyl-2-(5-phosphono-2-furanyl)imidazole 261366-74-9P, 2-Amino-5-propyl-4-(5-phosphono-2-furanyl)oxazole 261366-75-0P, 2-Amino-5-ethyl-4-(5-phosphono-2-furanyl)oxazole 261366-76-1P, 2-Amino-5-methyl-4-(5-phosphono-2-furanyl)oxazole 261366-77-2P, 2-Amino-4-(5-phosphono-2-furanyl)oxazole 261366-78-3P, 2-Amino-5-isobutyl-4-(5-phosphono-2-furanyl)oxazole monohydrobromide 261370-26-7P 261370-27-8P, 2-Methyl-5-isobutyl-4-(5-phosphorodiamido-2-furanyl)thiazole 261370-29-0P, 2-Amino-5-methylthio-4-(5-phosphorodiamido-2-furanyl)thiazole 261370-30-3P, 2-Amino-5-isobutyl-4-(5-phosphonomonoamido-2-furanyl)thiazole 261370-31-4P, 2-Amino-5-isobutyl-4-(5-phosphorodiamido-2-furanyl)thiazole 261370-32-5P, 2-Amino-5-isobutyl-4-[5-(N,N'-diisobutylphosphorodiamido)-2-furanyl]thiazole 261370-33-6P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1,3-bis(ethoxycarbonyl)-1-propyl]phosphorodiamido]-2-furanyl]thiazole 261370-34-7P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis((S)-1-benzyloxycarbonyl)ethyl]phosphorodiamido]-2-furanyl]thiazole 261370-35-8P 261370-39-2P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-((S)-1-methoxycarbonyl)ethyl]phosphonamido]-2-furanyl]thiazole 261370-44-9P, 2-Amino-5-isobutyl-4-[5-(O-phenylphosphonamido)-2-furanyl]thiazole 261370-46-1P, 2-Amino-5-isobutyl-4-(5-(O-phenyl-N-ethoxycarbonylmethylphosphonamido)-2-furanyl)thiazole 261370-48-3P, 2-Amino-5-isobutyl-4-(5-(O-phenyl-N-isobutylphosphonamido)-2-furanyl)thiazole 261370-50-7P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-((S)-1-ethoxycarbonyl-2-phenylethyl]phosphonamido)-2-furanyl]thiazole 261370-54-1P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-[(S)-1,3-bis(ethoxycarbonyl)propyl]phosphonamido]-2-furanyl]thiazole 261370-57-4P, 2-Amino-5-isobutyl-4-[5-[O-(3-chlorophenyl)-N-[(S)-1-(methoxycarbonyl)ethyl]phosphonamido]-2-furanyl]thiazole 261370-60-9P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-[1,1-bis(ethoxycarbonyl)methyl]phosphonamido]-2-furanyl]thiazole 261370-61-0P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-(1-morpholinyl)phosphonamido]-2-furanyl]thiazole 261370-62-1P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-[(S)-1-(benzyloxycarbonyl)ethyl]phosphonamido]-2-furanyl]thiazole 261370-63-2P, 2-Amino-5-isobutyl-4-(5-(O-

phenyl-N-benzyloxycarbonylmethylphosphonamido)-2-furanyl]thiazole  
 261370-64-3P, 2-Amino-5-isobutyl-4-[5-[O-(4-methoxyphenyl)-N-[(S)-1-(methoxycarbonyl)ethyl]phosphonamido]-2-furanyl]thiazole 261370-68-7P  
 261370-69-8P 261370-70-1P 261370-71-2P 261370-73-4P 261370-74-5P  
 261370-76-7P, 2-Amino-5-methylthio-4-(5-(N-methyl-1-phenyl-1,3-propylphosphonamido)-2-furanyl]thiazole 261370-79-0P,  
 2-Amino-5-isobutyl-4-[5-[[3-(3,5-dichlorophenyl)-1,3-propyl]phosphonamido]-2-furanyl]thiazole 261370-80-3P, 2-Amino-5-isobutyl-4-[5-(4,5-benzo-1-oxo-1-phospha-2-oxa-6-azacyclohexan-1-yl)-2-furanyl]thiazole  
 261372-35-4P, 2-Amino-4-phosphonomethyloxy-6-bromobenzothiazole  
 261372-36-5P, 2-Amino-4-phosphonomethyloxybenzothiazole 261372-38-7P,  
 2-Amino-4-phosphonomethyloxy-6-bromo-7-chlorobenzothiazole 261372-39-8P,  
 2-Amino-4-phosphonomethoxy-6-bromo-7-methylbenzothiazole 261372-40-1P,  
 2-Amino-4-phosphonomethoxy-7-methylbenzothiazole 261372-42-3P,  
 2-Amino-4-phosphonomethoxy-7-chlorobenzothiazole 261372-64-9P,  
 2-Amino-7-ethyl-6-thiocyano-4-phosphonomethoxybenzothiazole  
 261373-40-4P, 2-Methyl-5-ethyl-4-(5-phosphono-2-furanyl]thiazole  
 280779-70-6P, 2-Phenyl-5-isobutyl-4-(5-phosphono-2-furanyl]thiazole  
 280779-71-7P, 2-Amino-5-isopropyl-4-(5-phosphono-2-furanyl]thiazole  
 280779-72-8P, 2-Amino-5-methanesulfinyl-4-(5-phosphono-2-furanyl]thiazole  
 280779-74-0P, 2-Amino-5-(4-morpholinyl)methyl-4-(5-phosphono-2-furanyl]thiazole dihydrobromide 280779-79-5P, 2-Amino-5-ethyl-4-(5-phosphono-2-furanyl]selenazole 280779-91-1P, 2-Vinyl-5-isobutyl-4-(5-phosphono-2-furanyl]thiazole 280782-95-8P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis(benzyloxycarbonylmethyl)phosphonodiamido]furanyl]-2-thiazole  
 280782-96-9P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(R)-1-(methoxycarbonyl)ethyl]phosphonodiamido]furanyl]-2-thiazole  
 280782-97-0P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-(ethoxycarbonyl)ethyl]phosphonodiamido]furanyl]-2-thiazole 280782-98-1P,  
 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(tert-butoxycarbonyl)methyl]phosphonodiamido]furanyl]-2-thiazole 280782-99-2P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(ethoxycarbonyl)methyl]phosphonodiamido]furanyl]-2-thiazole  
 280783-00-8P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(1-methyl-1-ethoxycarbonyl)ethyl]phosphonodiamido]furanyl]-2-thiazole 280783-01-9P,  
 2-Amino-5-isobutyl-4-[5-[N,N'-bis(ethoxycarbonylmethyl)-N,N'-dimethylphosphonodiamido]-2-furanyl]thiazole 280783-02-0P,  
 2-Amino-5-isobutyl-4-[5-[N,N'-bis((S)-1-benzyloxycarbonyl-2-methylpropyl]phosphonodiamido)-2-furanyl]thiazole 280783-03-1P,  
 2-Amino-5-isobutyl-4-[5-[N,N'-bis((S)-1-methoxycarbonyl-3-methylbutyl]phosphonodiamido)-2-furanyl]thiazole 280783-04-2P,  
 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(R)-1-ethoxycarbonyl-2-(benzylthio)ethyl]phosphonodiamido]-2-furanyl]thiazole 280783-06-4P,  
 2-Amino-5-propylthio-4-[5-[N,N'-bis[(S)-1-(ethoxycarbonyl)ethyl]phosphonodiamido]-2-furanyl]thiazole 280783-07-5P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-benzyloxycarbonyl-2-methylisobutyl]phosphonodiamido]-2-furanyl]thiazole 280783-08-6P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-ethoxycarbonyl-3-methylbutyl]phosphonodiamido]-2-furanyl]thiazole  
 280783-09-7P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-ethoxycarbonyl-2-methylpropyl]phosphonodiamido]-2-furanyl]thiazole 280783-10-0P,  
 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-ethoxycarbonyl-2-phenylethyl]phosphonodiamido]-2-furanyl]thiazole 280783-11-1P,  
 2-Amino-5-propylthio-4-[5-[N,N'-bis[(1-methyl-1-ethoxycarbonyl)ethyl]phosphonodiamido]-2-furanyl]]thiazole 280783-12-2P,  
 2-Amino-5-methylthio-4-[5-[N,N'-bis[1-methyl-1-ethoxycarbonyl)ethyl]phosphonodiamido]-2-furanyl]thiazole 280783-13-3P,  
 2-Amino-5-isobutyl-4-[5-[N-morpholino-N'-[1-methyl-1-ethoxycarbonyl)ethyl]phosphonodiamido]-2-furanyl]thiazole 280783-14-4P,  
 2-Amino-5-isobutyl-4-[5-[N-pyrrolidino-N'-[1-methyl-1-ethoxycarbonyl)ethyl]phosphonodiamido]-2-furanyl]thiazole 347870-21-7P,  
 2-Amino-5-isobutyl-4-[5-[N,N'-bis((S)-1-ethoxycarbonylpropyl]phosphorodiam

ido]-2-furanyl]thiazole 347870-33-1P, 2-Amino-5-(2-thienyl)-4-(5-diethylphosphono-2-furanyl)thiazole 358670-36-7P, (5-(3,5-Dinitrophenyl)-2-furanyl)phosphonic acid 358670-37-8P, (5-(2-Amino-3,5-dinitrophenyl)-2-furanyl)phosphonic acid 358670-38-9P, (5-(5-Chloro-2-methoxyphenyl)-2-furanyl)phosphonic acid 358670-39-0P, (5-(2,5-Dichlorophenyl)-2-furanyl)phosphonic acid 358670-40-3P, (5-(2-Methylsulfamoyl-5-(trifluoromethyl)phenyl)-2-furanyl)phosphonic acid 358670-41-4P, (5-(5-Chloro-2-(methylsulfamoyl)phenyl)-2-furanyl)phosphonic acid 358670-42-5P, (5-(2-(Methylsulfamoyl)phenyl)-2-furanyl)phosphonic acid 358670-44-7P, (5-(2-Hydroxyphenyl)-2-furanyl)phosphonic acid 358670-45-8P, (5-(3,5-Dimethylphenyl)-2-furanyl)phosphonic acid 358670-46-9P, (5-(3-Bromophenyl)-2-furanyl)phosphonic acid 358670-47-0P, (5-(4-Aminophenyl)-2-furanyl)phosphonic acid 358670-48-1P, (5-(4-Chloro-2,5-dimethoxyphenyl)-2-furanyl)phosphonic acid 358670-49-2P, (5-(2-((4-Chlorobenzyl)carbamoyl)phenyl)-2-furanyl)phosphonic acid 358670-50-5P, (5-(2-((2-(4-Chlorophenyl)ethyl)carbamoyl)phenyl)-2-furanyl)phosphonic acid 358670-51-6P, (5-(2-(Benzylsulfamoyl)phenyl)-2-furanyl)phosphonic acid 358670-52-7P, (5-(2-Sulfamoylphenyl)-2-furanyl)phosphonic acid 358670-53-8P, (5-Pentamethylphenyl)-2-furanyl)phosphonic acid 358670-54-9P, (5-(2,3-Dicarboethoxyphenyl)-2-furanyl)phosphonic acid 358670-56-1P, (5-(4-Acetyl-amino-3-methylphenyl)-2-furanyl)phosphonic acid 358670-58-3P, (5-(2,4-Dichloro-6-methylphenyl)-2-furanyl)phosphonic acid 358670-59-4P, (5-(4-Hydroxy-2-carbomethoxyphenyl)-2-furanyl)phosphonic acid 358670-60-7P, (5-(2-Carbamoyl-4-methylphenyl)-2-furanyl)phosphonic acid 358670-61-8P, (5-(2-Ethoxycarbonyl-4-hydroxyphenyl)-2-furanyl)phosphonic acid 358670-62-9P, (5-(4-Nitrophenyl)-2-furanyl)phosphonic acid 358670-63-0P, (5-(2-((2,4-Difluorophenyl)carbamoyl)phenyl)-2-furanyl)phosphonic acid 358670-64-1P, (5-(3,5-Dichlorophenyl)-2-furanyl)phosphonic acid 358670-65-2P, (5-(3-Hydroxyphenyl)-2-furanyl)phosphonic acid 358670-66-3P, (5-(5-Bromo-3-carboxyphenyl)-2-furanyl)phosphonic acid 358670-67-4P, (5-(5-Formyl-2,3-dimethoxyphenyl)-2-furanyl)phosphonic acid 358670-68-5P, (5-(2-Nitrophenyl)-2-furanyl)phosphonic acid 358670-69-6P, (5-(Biphenyl-2-yl)-2-furanyl)phosphonic acid 358670-70-9P, (5-(2-(Carboethoxy)phenyl)-2-furanyl)phosphonic acid 358670-71-0P, (5-(4-Bromophenyl)-2-furanyl)phosphonic acid 358670-72-1P, (5-(3-Propanoylphenyl)-2-furanyl)phosphonic acid 358670-73-2P, (5-(5-Cyano-2-methoxyphenyl)-2-furanyl)phosphonic acid 358670-74-3P, (5-(2-Ethylphenyl)-2-furanyl)phosphonic acid 358670-75-4P, (5-(6-Methyl-2-nitrophenyl)-2-furanyl)phosphonic acid 358670-76-5P, (5-(4-(Acetyl-amino)phenyl)-2-furanyl)phosphonic acid 358670-77-6P, (5-(2,3,4,5-Tetramethylphenyl)-2-furanyl)phosphonic acid 358670-78-7P, (5-(Biphenyl-3-yl)-2-furanyl)phosphonic acid 358670-79-8P, (5-(5-Chloro-2-sulfamoylphenyl)-2-furanyl)phosphonic acid 358670-80-1P, (5-(4-((1-Pyrrolidinyl)acetyl)amino)phenyl)-2-furanyl)phosphonic acid 358670-81-2P, (5-(3,4-Dimethylphenyl)-2-furanyl)phosphonic acid 358670-82-3P, (5-(2,4-Dinitrophenyl)-2-furanyl)phosphonic acid 358670-83-4P, (5-(3-(Aminomethyl)phenyl)-2-furanyl)phosphonic acid 358670-84-5P, (5-(4-Amino-3-fluorophenyl)-2-furanyl)phosphonic acid 358670-85-6P, (5-(3-(Hydroxymethyl)phenyl)-2-furanyl)phosphonic acid 358670-86-7P, (5-(2-Bromophenyl)-2-furanyl)phosphonic acid 358670-87-8P, (5-(2-(2-Hydroxyethyl)phenyl)-2-furanyl)phosphonic acid 358670-88-9P, (5-(4-Carbamoylphenyl)-2-furanyl)phosphonic acid 358670-89-0P, (5-(4-Cyanophenyl)-2-furanyl)phosphonic acid 358670-90-3P, (5-(3-Cyanophenyl)-2-furanyl)phosphonic acid 358670-91-4P, (5-(2-Cyanophenyl)-2-furanyl)phosphonic acid 358670-92-5P, (5-(4-Amino-3-nitrophenyl)-2-furanyl)phosphonic acid 358670-93-6P, (5-(2-Isopropylphenyl)-2-furanyl)phosphonic acid 358670-94-7P, (5-(6-Amino-2-chloro-3-pyridyl)-2-furanyl)phosphonic acid 358670-95-8P,

(5-(2-Amino-5-chlorophenyl)-2-furanyl)phosphonic acid 358670-96-9P,  
 (5-(3-Chloro-5-fluorophenyl)-2-furanyl)phosphonic acid 358670-97-0P,  
 (5-(2-Methyl-5-nitrophenyl)-2-furanyl)phosphonic acid 358670-98-1P,  
 (5-(5-Fluoro-3-nitrophenyl)-2-furanyl)phosphonic acid 358670-99-2P,  
 (5-(2-Amino-5-carbomethoxyphenyl)-2-furanyl)phosphonic acid  
 358671-00-8P, (5-(2-Methoxy-5-nitrophenyl)-2-furanyl)phosphonic acid  
 358671-01-9P, (5-(2-Chloro-5-(trifluoromethyl)phenyl)-2-furanyl)phosphonic  
 acid 358671-02-0P, (5-(2,5-Bis(trifluoromethyl)phenyl)-2-  
 furanyl)phosphonic acid 358671-03-1P, (5-(4-Fluorophenyl)-2-  
 furanyl)phosphonic acid 358671-04-2P, (5-(2,4-Dichlorophenyl)-2-  
 furanyl)phosphonic acid 358671-05-3P, (5-(3-Amino-5-carbomethoxyphenyl)-  
 2-furanyl)phosphonic acid 358671-06-4P, (5-(3-Amino-4-bromophenyl)-2-  
 furanyl)phosphonic acid 358672-11-4P, (5-(4-Methyl-3-thienyl)-2-  
 furanyl)phosphonic acid 389057-32-3P, (5-(2-(Propylsulfamoyl)phenyl)-2-  
 furanyl)phosphonic acid 389057-53-8P 389057-54-9P,  
 2-Amino-5-ethylthiocarbonyl-4-(5-phosphono-2-furanyl)thiazole  
 389057-55-0P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)thiazole  
 N,N-dicyclohexylammonium salt 389057-73-2P, 2-Amino-5-isobutyl-4-[5-[O-  
 (4-chlorophenyl)-N-((S)-1-methoxycarbonylethyl)phosphonamido]-2-  
 furanyl]thiazole 389057-74-3P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-[2-  
 (ethoxycarbonyl)propyl]phosphonamido]-2-furanyl]thiazole 389057-76-5P,  
 2-Amino-4-[[3-(3,5-dichlorophenyl)propane-1,3-diyl]phosphonomethoxy]-  
 6,7,8,9-tetrahydronaphtho[1,2-d]thiazole  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(combination of phosphonate or phosphorodiamidate FBPase  
 inhibitors and antidiabetic agents useful for treatment of  
 diabetes)

IT 213124-93-7 213199-10-1 213247-37-1 240434-61-1 280783-15-5  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(combination of phosphonate or phosphorodiamidate FBPase  
 inhibitors and antidiabetic agents useful for treatment of  
 diabetes)

IT 213190-65-9, Exendin  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(exendin and exendin agonists, insulin secretagogue; combination of  
 phosphonate or phosphorodiamidate FBPase inhibitors and  
 antidiabetic agents useful for treatment of diabetes)

IT 9004-10-8, Insulin, biological studies 116094-23-6, Insulin aspart  
 133107-64-9, Insulin lispro 160337-95-1, Insulin glargine  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(in combination with phosphonate or phosphorodiamidate FBPase  
 inhibitors useful for treatment of diabetes)

IT 9001-39-2, Glucose-6-phosphatase 9001-42-7,  $\alpha$ -Glucosidase  
 9001-52-9, Fructose bisphosphatase 9035-74-9, Glycogen phosphorylase  
 54249-88-6, Dipeptidyl peptidase-IV  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors; combination of phosphonate or phosphorodiamidate  
 FBPase inhibitors and antidiabetic agents useful for  
 treatment of diabetes)

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 114-86-3, Phenformin  
 451-71-8, Glyhexamide 657-24-9, Metformin 664-95-9, Tolcyclamide  
 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide  
 3149-00-6, Phenbutamide 10238-21-8, Glyburide 21187-98-4, Glipizide  
 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide  
 33342-05-1, Gliquidone 56180-94-0, Acarbose 72432-03-2, Miglitol

83480-29-9, Voglibose 93479-97-1, Glimepiride 105816-04-4, Nateglinide  
 135062-02-1, Repaglinide 145375-43-5, Mitiglinide  
 161748-40-9, BTS-67582 204656-20-2, NN 2211 247016-69-9, NVP-DPP728  
 251572-86-8, P 32/98

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(insulin secretagogue; combination of phosphonate or phosphorodiamidate  
 FBPase inhibitors and antidiabetic agents useful for  
 treatment of diabetes)

IT 261373-15-3P, 2-Methyl-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic  
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); RACT (Reactant or reagent); USES (Uses)

(intermediate; combination of phosphonate or phosphorodiamidate FBPase  
 inhibitors and antidiabetic agents useful for treatment of  
 diabetes)

IT 1738-68-7, Benzyl aminoacetate 358672-65-8, 6-Amino-2-chloro-3-  
 bromopyridine

RL: RCT (Reactant); RACT (Reactant or reagent)

(intermediate; combination of phosphonate or phosphorodiamidate FBPase  
 inhibitors and antidiabetic agents useful for treatment of  
 diabetes)

IT 36366-55-9P, Diethyl 2-furanylphosphonate 78072-59-0P,  
 2-(4-Methyl-1-oxopentyl)furan 82619-14-5P, Ethoxycarbonyloxymethyl  
 iodide 104208-14-2P 213124-94-8P, 5-Diethylphosphono-2-furaldehyde  
 261372-78-5P, 2-Bromo-5-isobutyl-4-(5-diethylphosphono-2-furanyl)thiazole  
 261373-31-3P, 2-Diethylphosphonomethoxy-5-bromonitrobenzene  
 389057-77-6P, 4-Phosphonomethoxy-6,7,8,9-tetrahydronaphtho[1,2-d]thiazole  
 dichloridate

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(intermediate; combination of phosphonate or phosphorodiamidate FBPase  
 inhibitors and antidiabetic agents useful for treatment of  
 diabetes)

IT 953-18-4P, (R)-Ethyl 2-amino-3-(benzylthio)propanoate 2666-93-5P,  
 L-Leucine methyl ester 2743-60-4P, L-Leucine ethyl ester 3081-24-1P,  
 L-Phenylalanine ethyl ester 13200-60-7P, N-Methylglycine ethyl ester  
 17431-03-7P, L-Valine ethyl ester 21760-98-5P, L-Valine benzyl ester  
 154092-64-5P, (S)-Benzyl 2-amino-3,3-dimethylbutanoate

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(reactant; combination of phosphonate or phosphorodiamidate FBPase  
 inhibitors and antidiabetic agents useful for treatment of  
 diabetes)

IT 78-81-9, Isobutylamine 88-67-5, 2-Iodobenzoic acid 98-01-1,  
 2-Furaldehyde, reactions 109-80-8, 1,3-Propanedithiol 110-00-9, Furan  
 110-70-3, N,N'-Dimethylethylenediamine 354-37-0, Trifluoroacetamidine  
 431-03-8, 2,3-Butanedione 459-73-4, Glycine ethyl ester 533-58-4,  
 2-Iodophenol 540-37-4, 4-Iodoaniline 583-55-1, 2-Bromo-1-iodobenzene  
 589-87-7, 1-Bromo-4-iodobenzene 591-18-4, 1-Bromo-3-iodobenzene  
 609-73-4, 1-Iodo-2-nitrobenzene 622-50-4, 4-Iodoacetanilide 623-00-7,  
 4-Bromobenzonitrile 626-02-8, 3-Iodophenol 636-98-6,  
 1-Iodo-4-nitrobenzene 646-07-1, 4-Methylpentanoic acid 672-57-1,  
 2-Chloro-1-iodo-5-trifluoromethylbenzene 696-40-2, 3-Iodobenzylamine  
 709-49-9, 1-Iodo-2,4-dinitrobenzene 814-49-3, Diethyl chlorophosphate  
 873-38-1, 2-Bromo-4-chloroaniline 875-51-4, 4-Bromo-2-nitroaniline  
 1074-16-4, 2-Bromophenethyl alcohol 1113-49-1, Ethyl  
 2-amino-2-methylpropanoate 1115-59-9, L-Alanine ethyl ester,  
 hydrochloride 1459-01-4, 2-Iodoisopropylbenzene 1765-93-1,

4-Fluorophenylboronic acid 1817-73-8, 2-Bromo-4,6-dinitroaniline  
 2042-37-7, 2-Bromobenzonitrile 2113-51-1, 2-Iodobiphenyl 2113-57-7,  
 3-Bromobiphenyl 2491-20-5, L-Alanine methyl ester hydrochloride  
 3032-81-3, 3,5-Dichloriodobenzene 3082-75-5, L-Alanine ethyl ester  
 3819-88-3, 3-Nitro-5-fluoro-1-iodobenzene 3853-91-6,  
 1-Iodo-2,3,4,5,6-pentamethylbenzene 3956-07-8, 4-Iodobenzamide  
 5197-28-4, 2-Bromo-4-nitroanisole 5464-79-9, 2-Amino-4-  
 methoxybenzothiazole 6456-74-2 6937-34-4, 3-Iodophthalic acid  
 6948-30-7, 3-Bromo-4,5-dimethoxybenzaldehyde 6952-59-6,  
 3-Bromobenzonitrile 7051-34-5, Cyclopropanemethyl bromide 7617-93-8,  
 1-Bromo-2,5-bis(trifluoromethyl)benzene 7745-93-9, 2-Bromo-4-  
 nitrotoluene 13529-27-6, 2-Furaldehyde diethyl acetal 16450-41-2,  
 L-Glutamic acid diethyl ester 17831-01-5, L-Alanine benzyl ester  
 18282-40-1, 1-Ethyl-2-iodobenzene 19718-49-1, 2-Iodo-4-  
 carbomethoxyaniline 19829-31-3, 3'-Bromopropiophenone 21705-13-5,  
 D-Alanine methyl ester 22445-41-6, 5-Iodo-m-xylene 29632-74-4,  
 2-Fluoro-4-iodoaniline 29682-41-5, 2,5-Dichloro-1-iodobenzene  
 30318-99-1, 3-Bromo-4-methylthiophene 31599-61-8, 3,4-  
 Dimethyliodobenzene 33863-76-2, 1-Bromo-3-chloro-5-fluorobenzene  
 41085-43-2, 2-Bromo-3-nitrotoluene 45644-21-1, 6-Amino-2-chloropyridine  
 52807-27-9, 4-Chloro-2-iodoanisole 53730-99-7, 2-Iodobenzenesulfonamide  
 54509-71-6, 2,3,4,5-Tetramethyliodobenzene 57455-06-8, 3-Iodobenzyl  
 alcohol 57772-57-3, 5-Hydroxy-2-iodobenzoic acid 63980-69-8,  
 1-(2-Methoxy-5-chlorophenyl)thiourea 68716-47-2, 2,4-  
 Dichlorophenylboronic acid 85006-23-1, 3-Aminophenylboronic acid  
 hydrochloride 90064-46-3, 2,5-Dimethoxy-4-iodochlorobenzene  
 106938-62-9, Diethylphosphonomethyl trifluoromethylsulfonate  
 117324-09-1, 4-Iodo-2-methylacetanilide 117572-79-9,  
 3-Bromo-4-methoxybenzonitrile 118486-94-5, 2-Tributylstannylfuran  
 125259-03-2, N-Methyl-2-iodobenzenesulfonamide 175277-97-1,  
 3,5-Dichloro-2-iodotoluene 188815-32-9, 3-Bromo-5-iodobenzoic acid  
 261369-11-3, 2-Amino-5-isobutyl-4-(5-diphenylphosphono-2-furanyl)thiazole  
 261372-76-3, 2-Amino-5-isobutyl-4-(5-diethylphosphono-2-furanyl)thiazole  
 261372-77-4, 2-Amino-5-bromo-4-(5-diethylphosphono-2-furanyl)thiazole  
 261373-39-1, 3-(3,5-Dichlorophenyl)-1,3-propanediol 270086-79-8,  
 N-(4-Iodophenyl)-2-(tetrahydro-1H-pyrrol-1-yl)acetamide 271796-28-2,  
 4-Chloro-2-iodobenzenesulfonamide 271796-61-3, N-Benzyl-2-  
 iodobenzenesulfonamide 271796-68-0, N-Propyl-4-chloro-2-  
 iodobenzenesulfonamide 273208-13-2, N-Methyl-2-iodo-4-  
 (trifluoromethyl)benzenesulfonamide 273208-16-5, N-Methyl-4-chloro-2-  
 iodobenzenesulfonamide 304644-56-2, N-(4-Chlorobenzyl)-2-iodobenzamide  
 309253-36-9, 2-Iodo-5-methylbenzamide 347869-08-3, 5-Diethylphosphono-2-  
 (2-bromo-4-methyl-1-oxopentyl)furan 347869-10-7, 5-Diethylphosphono-2-  
 (bromoacetyl)furan 347869-19-6, Diethyl (5-iodo-2-furanyl)phosphonate  
 349110-34-5, N-(2,4-Difluorophenyl)-2-iodobenzamide 358672-63-6,  
 N-(4-Chlorophenethyl)-2-iodobenzamide 358672-64-7, Methyl  
 5-hydroxy-2-iodobenzoate 380430-56-8, 3-Amino-5-  
 carbomethoxyphenylboronic acid 389057-75-4, 2-Amino-4-phosphonomethoxy-  
 6,7,8,9-tetrahydronaphtho[1,2-d]thiazole 389057-78-7,  
 4-Diphenylphosphonomethoxy-6,7,8,9-tetrahydronaphtho[1,2-d]thiazole  
 389057-79-8, 4-Phenylphosphonomethoxy-6,7,8,9-tetrahydronaphtho-[1,2-  
 d]thiazole 389057-80-1, 4-Phosphonomethoxy-6,7,8,9-tetrahydronaphtho[1,2-  
 d]thiazole  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reactant; combination of phosphonate or phosphorodiamidate FBPase  
 inhibitors and antidiabetic agents useful for treatment of  
 diabetes)



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DOCUMENT NUMBER: 138:265470  
TITLE: Study of the insulinotropic effect of the novel antihyperglycemic agent KAD-1229 using HIT T15 cells, a hamster's insulinoma cell line  
AUTHOR(S): Ichikawa, Kiyoshi; Yamato, Tokuhisa; Tsuji, Atsutoshi; Ojima, Kazuma; Kusama, Hiroshi; Kojima, Masami  
CORPORATE SOURCE: Pharmacology Research, Research & Development, Kissei Pharmaceutical Co., Ltd., Hotaka, Nagano, Japan  
SOURCE: Arzneimittel-Forschung (2002), 52(8), 605-609  
CODEN: ARZNAD; ISSN: 0004-4172  
PUBLISHER: Editio Cantor Verlag  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
ED Entered STN: 02 Oct 2002  
AB The insulinotropic effect of (+)-monocalcium bis [(2S)-2-benzyl-3-(cis-hexahydro-2-isoindoliny1-carbonyl)propionate]dihydrate (CAS 145375-43-5, KAD-1229) was assessed by comparing it with those of glibenclamide (CAS 10238-21-8), nateglinide (CAS 105816-04-4), and repaglinide (CAS 135062-02-1) using HIT T15 cells, a hamster insulinoma cell line. Although their potencies were different, KAD-1229, glibenclamide, nateglinide, and repaglinide all concentration-dependently and significantly induced insulin release from these cells. Further, each agent displaced the binding of 3H-glibenclamide to the cell membrane and inhibited 86Rb+ efflux from the cells. These results indicate that KAD-1229, glibenclamide, nateglinide, and repaglinide each exert their insulinotropic effect by binding to the glibenclamide binding sites (sulfonylurea receptors) on pancreatic  $\beta$ -cells and closing K+ channels. Diazoxide, a K+ channel opener, and nitrendipine, a Ca2+ blocker, suppressed the insulin release induced by KAD-1229 or glibenclamide. These results demonstrate that the insulinotropic actions of KAD-1229 and glibenclamide involve similar underlying pathways.  
CC 1-10 (Pharmacology)  
ST antihyperglycemic KAD1229 insulinotrope pancreas beta cell diabetes mellitus; nateglinide repaglinide glibenclamide hypoglycemic KAD1229 diabetes; insulin secretagogue K channel calcium blocker sulfonylurea receptor antidiabetic  
IT Antidiabetic agents  
Diabetes mellitus  
(mechanism of antihyperglycemic agent KAD-1229 insulinotropic effect on hamster pancreatic  $\beta$ -cells)  
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 23 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2001:635931 HCAPLUS Full-text  
DOCUMENT NUMBER: 135:185506  
TITLE: Antidiabetic agents containing  $\alpha$ -glucosidase inhibitors and insulin secretion promoters  
INVENTOR(S): Sugiyama, Yasuo; Odaka, Hiroyuki; Sakiyama, Hiroshi; Iwasaki, Masato; Funatsu, Masami  
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan  
SOURCE: PCT Int. Appl., 25 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001062295      A1      20010830      WO 2001-JP1282      20010222 <--
W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
    CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
    HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU,
    LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
    SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
    ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW:  GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
    DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
    BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2401356          A1      20010830      CA 2001-2401356      20010222 <--
AU 2001034114       A5      20010903      AU 2001-34114        20010222 <--
EP 1295609          A1      20030326      EP 2001-906193       20010222 <--
R:   AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
    IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2001316293       A       20011113      JP 2001-47695        20010223 <--
US 2003040490       A1      20030227      US 2002-204783       20020821 <--
PRIORITY APPLN. INFO.:      JP 2000-52297      A  20000224 <--
                               WO 2001-JP1282      W  20010222 <--

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ED Entered STN: 31 Aug 2001

AB Drugs containing, as the active ingredients, exclusively a combination of an  $\alpha$ -glucosidase inhibitor with a non-sulfonylurea insulin secretion promoter, are useful as preventives and remedies for diabetes, etc. Diabetic patients were administered with a tablet containing 0.2 mg voglibose and a tablet containing 2 mg repaglinide before breakfast and blood samples were taken 1 h after meals and the results showed a significant decrease in blood glucose levels.

IC ICM A61K045-06

ICS A61K031-44; A61K031-405; A61K031-198; A61K031-702; A61K031-133; A61K031-70; A61P003-10; A61P043-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST antidiabetic glucosidase inhibitor insulin secretion promoter;  
voglibose repaglinide diabetes control

IT Antidiabetic agents

(antidiabetic agents containing  $\alpha$ -glucosidase inhibitors  
and insulin secretion promoters)

IT Drug delivery systems

(tablets; antidiabetic agents containing  $\alpha$ -glucosidase  
inhibitors and insulin secretion promoters)

IT 56180-94-0, Acarbose 72432-03-2, Miglitol 80879-63-6, Emiglitate  
83480-29-9, Voglibose 105816-04-4, Nateglinide 135062-02-1,  
Repaglinide 145375-43-5, Mitiglinide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antidiabetic agents containing  $\alpha$ -glucosidase inhibitors  
and insulin secretion promoters)

IT 9001-42-7,  $\alpha$ -Glucosidase 9004-10-8, Insulin, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(antidiabetic agents containing  $\alpha$ -glucosidase inhibitors  
and insulin secretion promoters)

IT 50-99-7, D-Glucose, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

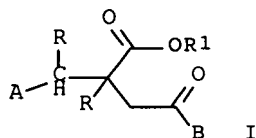
(blood; antidiabetic agents containing  $\alpha$ -glucosidase  
inhibitors and insulin secretion promoters)

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REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 24 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2000:814308 HCAPLUS Full-text  
 DOCUMENT NUMBER: 133:359230  
 TITLE: Use of succinic acid derivatives to obtain a medicine for treating inflammation  
 INVENTOR(S): Caille, Dominique  
 PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.  
 SOURCE: PCT Int. Appl., 13 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067752	A1	20001116	WO 2000-FR1246	20000509 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2793411	A1	20001117	FR 1999-5978	19990511 <--
FR 2793411	B1	20010629		
EP 1178794	A1	20020213	EP 2000-927322	20000509 <--
EP 1178794	B1	20050907		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002544163	T	20021224	JP 2000-616778	20000509 <--
AT 303807	T	20050915	AT 2000-927322	20000509 <--
PRIORITY APPLN. INFO.:			FR 1999-5978	A 19990511 <--
			WO 2000-FR1246	W 20000509 <--
OTHER SOURCE(S): MARPAT 133:359230				
ED Entered STN: 21 Nov 2000				
GI				



AB The invention concerns the use of succinic acid derivs. of general formula (I) wherein: A represents a Ph group optionally substituted by one, two or three substituents selected among a halogen, a C1-6 alkyl, C1-6 alkoxy group; a Ph, furyl, pyridyl or cycloalkyl with 3 to 8 carbon atoms; B represents an aminobicyclic group which consists of an amino cyclic compound with 5 or 6 members condensed with a cycloalkyl ring with 5 or 6 members which may have 1 or 2 unsatd. bonds, provided that B is bound to the carbon atom of the

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carbonyl group on the nitrogen atom; each R represents a hydrogen atom and all the R radicals are combined together to form a chemical bond; R1 represents a hydrogen atom, a C1-6 alkyl group, an aralkyl group with 7 to 10 carbon atoms; when there exist geometric isomers, each geometric isomer, the isomers E and the isomers Z thereof, the isomers trans and the isomers cis, for treating inflammation. The compns. are administered at a daily dose of 1-100 mg orally, or 0.1-100 mg parenterally ( no data).

IC ICM A61K031-4035

ICS A61P029-00

CC 1-7 (Pharmacology)

ST succinic acid deriv inflammation inhibitor

IT Nerve, disease

(diabetic neuropathy; use of succinic acid derivs. to obtain medicine for treating inflammation)

IT Arthritis

(polyarthritis, inhibitors; use of succinic acid derivs. to obtain medicine for treating inflammation)

IT 110-15-6D, Succinic acid, derivs. 145375-43-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of succinic acid derivs. to obtain medicine for treating inflammation)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 161 25-49 ibib ab ind

L61 ANSWER 25 OF 49 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2005331235 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 15981944  
TITLE: Pharmacology of the meglitinide analogs: new treatment options for type 2 diabetes mellitus.  
AUTHOR: Malaisse Willy J  
CORPORATE SOURCE: Laboratory of Experimental Hormonology, Brussels Free University, Brussels, Belgium.. malaisse@ulb.ac.be  
SOURCE: Treatments in endocrinology, (2003) Vol. 2, No. 6, pp. 401-14. Ref: 83  
Journal code: 101132977. ISSN: 1175-6349.  
PUB. COUNTRY: New Zealand  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200507  
ENTRY DATE: Entered STN: 29 Jun 2005  
Last Updated on STN: 13 Jul 2005  
Entered Medline: 12 Jul 2005

AB The expression meglitinide analogs was introduced in 1995 to cover new molecules proposed as non-sulfonylurea insulinotropic agents and displaying structural analogy with meglitinide, such as repaglinide, nateglinide, and mitiglinide. Meglitinide analogs display, as judged by conformation analysis, a U-shaped configuration similar to that of antihyperglycemic sulfonylureas such as glibenclamide (glyburide) and glimepiride. In rat pancreatic islets incubated in the presence of 7.0 mmol/L D-glucose, repaglinide and mitiglinide demonstrate comparable concentration-response relationships for stimulation of insulin release, with a threshold value < 10 nmol/L and a maximal secretory response at about 10 nmol/L. Several findings indicate that meglitinide analogs provoke the closing of adenosine triphosphate-sensitive potassium

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channels, with subsequent gating of voltage-sensitive calcium channels. The effects of meglitinide analogs upon the binding of [3H]glibenclamide to islet cells membranes reinforces this concept. At variance, however, with other meglitinide analogs, the ionic and secretory response to repaglinide (10 micromol/L) is not rapidly reversible in perfused rat islets. In experiments conducted in vivo in control and diabetic rats, repaglinide provokes a greater and more rapid increase in plasma insulin concentration and an earlier fall in glycemia than glibenclamide or glimepiride. Onset of effect is also more rapid and duration of effect shorter with nateglinide versus glibenclamide. In clinical studies, single or repeated daily administration of repaglinide increased plasma insulin concentration in a dose-dependent manner, with an incremental peak reached about 2 hours after repaglinide intake. Plasma concentrations of repaglinide are about 5.0 microg/L 2-2.5 hours after oral intake of the drug. Despite the slow reversibility of repaglinide action in vitro, this drug offers advantages over glibenclamide in terms of the possible occurrence of hypoglycemia if a meal is missed. In volunteers receiving a single oral dose of nateglinide (120mg) 10 minutes before a standardized 800 Kcal breakfast, the plasma insulin concentration was higher 5, 10, and 20 minutes after meal intake than when they received a single dose of repaglinide (0.5 or 2.0mg) or placebo 10 minutes before breakfast. Peak plasma concentrations of nateglinide were reached within 2 hours in most volunteers. Peak plasma concentrations of mitiglinide were reached 30 minutes after a single oral dose in a representative volunteer. Mitiglinide significantly suppressed meal-induced elevations in blood glucose concentrations in a study of patients with type 2 diabetes. In conclusion, two obvious differences among these meglitinide analogs should be underlined. First, on a molar basis, nateglinide is somewhat less potent than repaglinide or mitiglinide, as an insulinotropic agent. The maximal secretory responses evoked by these three meglitinide analogs are, however, identical to one another. Secondly, and as already mentioned, the functional effects of nateglinide and mitiglinide are more rapidly reversible than those of repaglinide, for instance in perfused rat islets. The meglitinide analogs offer the advantage over the long-acting antihyperglycemic sulfonylurea glibenclamide of minimizing the risk of undesirable hypoglycemia.

CT Animals

- \*Benzamides: TU, therapeutic use
- \*Carbamates: TU, therapeutic use
- \*Cyclohexanes: TU, therapeutic use
- \*Diabetes Mellitus, Type 2: DT, drug therapy

Humans

- \*Hypoglycemic Agents: TU, therapeutic use
- \*Phenylalanine: AA, analogs & derivatives
- \*Phenylalanine: TU, therapeutic use
- \*Piperidines: TU, therapeutic use

RN 105816-04-4 (nateglinide); 135062-02-1 (repaglinide); 54870-28-9 (meglitinide); 63-91-2 (Phenylalanine)

CN 0 (Benzamides); 0 (Carbamates); 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Piperidines)

L61 ANSWER 26 OF 49

MEDLINE on STN

DUPLICATE 3

ACCESSION NUMBER: 2002271275 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12010187

TITLE: Effect of KAD-1229, a novel hypoglycaemic agent, on plasma glucose levels after meal load in type 2 diabetic rats.

AUTHOR: Ichikawa Kiyoshi; Yamato Tokuhisa; Ojima Kazuma; Tsuji Atsutoshi; Ishikawa Kohtarō; Kusama Hiroshi; Kojima Masami

CORPORATE SOURCE: Pharmacology Laboratories, Kissei Pharmaceutical Co. Ltd, Hotaka, Nagano, Japan.. kiyoshi\_ichikawa@pharm.kissei.co.jp

SOURCE: Clinical and experimental pharmacology & physiology,

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(2002 May-Jun) Vol. 29, No. 5-6, pp. 423-7.

Journal code: 0425076. ISSN: 0305-1870.

PUB. COUNTRY: Australia  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200208  
ENTRY DATE: Entered STN: 16 May 2002  
Last Updated on STN: 30 Aug 2002  
Entered Medline: 29 Aug 2002

AB 1. The effects of KAD-1229 (a novel non-sulphonylurea agent), voglibose (an alpha-glucosidase inhibitor) and nateglinide (a non-sulphonylurea antihyperglycaemic agent) on hyperglycaemia induced by a meal load were assessed in diabetic rats. 2. KAD-1229 suppressed the increase in plasma glucose levels seen after a meal load and the area under the curve for plasma glucose levels (AUCglucose) up to 5 h after the meal load. 3. Voglibose also suppressed the increase in plasma glucose levels; however, a significant decrease in AUCglucose following voglibose was not observed. 4. Nateglinide suppressed the increase in plasma glucose levels at 30 min and 1 h after the meal load; however, plasma glucose levels was above control thereafter and the AUCglucose was not decreased. 5. The results indicate that KAD-1229 has an antihyperglycaemic effect and KAD-1229 is suggested to be a suitable agent for controlling post-prandial hyperglycaemia.

CT Animals

\*Blood Glucose: ME, metabolism

Cyclohexanes: PD, pharmacology

Diabetes Mellitus, Experimental: BL, blood

\*Diabetes Mellitus, Experimental: DT, drug therapy

Diabetes Mellitus, Type 2: BL, blood

\*Diabetes Mellitus, Type 2: DT, drug therapy

Food

\*Hypoglycemic Agents: PD, pharmacology

\*Indoles: PD, pharmacology

\*Inositol: AA, analogs & derivatives

Inositol: PD, pharmacology

\*Phenylalanine: AA, analogs & derivatives

Phenylalanine: PD, pharmacology

\*Postprandial Period

Rats

Rats, Wistar

Species Specificity

RN 105816-04-4 (nateglinide); 63-91-2 (Phenylalanine); 6917-35-7 (Inositol);  
83480-29-9 (voglibose)

CN 0 (Blood Glucose); 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles);  
0 (mitiglinide)

L61 ANSWER 27 OF 49

MEDLINE on STN

DUPLICATE 4

ACCESSION NUMBER: 2001260288 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11264248

TITLE: Effects of mitiglinide (S 21403) on Kir6.2/SUR1,  
Kir6.2/SUR2A and Kir6.2/SUR2B types of ATP-sensitive  
potassium channel.

AUTHOR: Reimann F; Proks P; Ashcroft F M

CORPORATE SOURCE: University Laboratory of Physiology, Parks Road, Oxford OX1  
3PT.

SOURCE: British journal of pharmacology, (2001 Apr) Vol.  
132, No. 7, pp. 1542-8.

Journal code: 7502536. ISSN: 0007-1188.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

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(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200105  
ENTRY DATE: Entered STN: 21 May 2001  
Last Updated on STN: 21 May 2001  
Entered Medline: 17 May 2001

AB 1. We have investigated the mechanism of action of the novel anti-diabetic agent mitiglinide (S 21403) on Kir6.2/SUR1, Kir6.2/SUR2A and Kir6.2/SUR2B types of ATP-sensitive potassium (K(ATP)) channel. These possess a common pore-forming subunit, Kir6.2, and different regulatory sulphonylurea receptor (SUR) subunits. It is believed that they correspond to native K(ATP) channels in pancreatic beta-cells, heart and non-vascular smooth muscle, respectively. 2. Kir6.2 was coexpressed with SUR1, SUR2A or SUR2B in *Xenopus* oocytes and macroscopic currents were recorded in giant inside-out membrane patches. Mitiglinide was added to the intracellular membrane surface. 3. Mitiglinide inhibited Kir6.2/SUR currents at two sites: a low-affinity site on Kir6.2 and a high-affinity site on SUR. Low-affinity inhibition was similar for all three types of K(ATP) channel but high-affinity inhibition was greater for Kir6.2/SUR1 currents (IC(50), 4 nM) than for Kir6.2/SUR2A or Kir6.2/SUR2B currents (IC(50), 3 and 5 microM, respectively). 4. Inhibition of Kir6.2/SUR1 currents was only slowly reversible on the time scale of electrophysiological experiments. 5. Kir6.2/SUR1-S1237Y currents, which previously have been shown to lack high affinity tolbutamide inhibition, resembled Kir6.2/SUR2 currents in being unaffected by 100 nM but blocked by 10 microM mitiglinide. 6. Our results show that mitiglinide is a high-affinity drug that shows a 1000 fold greater affinity for the beta-cell type than the cardiac and smooth muscle types of K(ATP) channel, when measured in excised patches.

CT Check Tags: Female  
\*Adenosine Triphosphate: PH, physiology  
Animals  
Dose-Response Relationship, Drug  
\*Indoles: PD, pharmacology  
Membrane Potentials: DE, drug effects  
Mice  
\*Potassium Channels: DE, drug effects  
Potassium Channels: GE, genetics  
Potassium Channels: PH, physiology  
\*Potassium Channels, Inwardly Rectifying  
Protein Subunits  
RNA, Messenger: AD, administration & dosage  
RNA, Messenger: GE, genetics  
*Xenopus laevis*

RN 56-65-5 (Adenosine Triphosphate)

CN 0 (Indoles); 0 (Potassium Channels); 0 (Potassium Channels, Inwardly Rectifying); 0 (Protein Subunits); 0 (RNA, Messenger); 0 (mitiglinide)

L61 ANSWER 28 OF 49 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 2001689244 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11716850

TITLE: The effects of mitiglinide (KAD-1229), a new anti-diabetic drug, on ATP-sensitive K<sup>+</sup> channels and insulin secretion: comparison with the sulfonylureas and nateglinide.

AUTHOR: Sunaga Y; Gono T; Shibasaki T; Ichikawa K; Kusama H; Yano H; Seino S

CORPORATE SOURCE: Department of Cellular and Molecular Medicine, Graduate School of Medicine, Chiba University 1-8-1 Inohana, Chuo-ku, 260-8670, Chiba, Japan.

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SOURCE: European journal of pharmacology, (2001 Nov 9)  
Vol. 431, No. 1, pp. 119-25.  
Journal code: 1254354. ISSN: 0014-2999.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200201  
ENTRY DATE: Entered STN: 11 Dec 2001  
Last Updated on STN: 25 Jan 2002  
Entered Medline: 11 Jan 2002

AB Mitiglinide (KAD-1229), a new anti-diabetic drug, is thought to stimulate insulin secretion by closing the ATP-sensitive K<sup>+</sup> (K(ATP)) channels in pancreatic beta-cells. However, its selectivity for the various K(ATP) channels is not known. In this study, we examined the effects of mitiglinide on various cloned K(ATP) channels (Kir6.2/SUR1, Kir6.2/SUR2A, and Kir6.2/SUR2B) reconstituted in COS-1 cells, and compared them to another meglitinide-related compound, nateglinide. Patch-clamp analysis using inside-out recording configuration showed that mitiglinide inhibits the Kir6.2/SUR1 channel currents in a dose-dependent manner (IC<sub>50</sub> value, 100 nM) but does not significantly inhibit either Kir6.2/SUR2A or Kir6.2/SUR2B channel currents even at high doses (more than 10 microm). Nateglinide inhibits Kir6.2/SUR1 and Kir6.2/SUR2B channels at 100 nM, and inhibits Kir6.2/SUR2A channels at high concentrations (1 microm). Binding experiments on mitiglinide, nateglinide, and repaglinide to SUR1 expressed in COS-1 cells revealed that they inhibit the binding of [3H]glibenclamide to SUR1 (IC<sub>50</sub> values: mitiglinide, 280 nM; nateglinide, 8 microm; repaglinide, 1.6 microm), suggesting that they all share a glibenclamide binding site. The insulin responses to glucose, mitiglinide, tolbutamide, and glibenclamide in MIN6 cells after chronic mitiglinide, nateglinide, or repaglinide treatment were comparable to those after chronic tolbutamide and glibenclamide treatment. These results indicate that, similar to the sulfonylureas, mitiglinide is highly specific to the Kir6.2/SUR1 complex, i.e., the pancreatic beta-cell K(ATP) channel, and suggest that mitiglinide may be a clinically useful anti-diabetic drug.

CT \*ATP-Binding Cassette Transporters  
Animals  
COS Cells  
Cell Line  
Cyclohexanes: PD, pharmacology  
Glyburide: PD, pharmacology  
\*Hypoglycemic Agents: PD, pharmacology  
\*Indoles: PD, pharmacology  
\*Insulin: ME, metabolism  
Patch-Clamp Techniques  
\*Phenylalanine: AA, analogs & derivatives  
Phenylalanine: PD, pharmacology  
Potassium Channels: GE, genetics  
\*Potassium Channels: ME, metabolism  
\*Potassium Channels, Inwardly Rectifying  
Receptors, Drug: GE, genetics  
Receptors, Drug: ME, metabolism  
Sulfonylurea Compounds: PD, pharmacology  
Tolbutamide: PD, pharmacology  
Transfection

RN 10238-21-8 (Glyburide); 105816-04-4 (nateglinide); 11061-68-0 (Insulin);  
63-91-2 (Phenylalanine); 64-77-7 (Tolbutamide)

CN 0 (ATP-Binding Cassette Transporters); 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Potassium Channels); 0 (Potassium Channels,



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Inwardly Rectifying); 0 (Receptors, Drug); 0 (Sulfonylurea Compounds); 0 (mitiglinide); 0 (sulfonylurea receptor)

L61 ANSWER 29 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2006653767 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 17087304

TITLE: Glinide(s), sulfonylurea(s).

AUTHOR: Arakawa Masayuki; Hirose Takahisa

CORPORATE SOURCE: Department of Medicine, Metabolism and Endocrinology, Juntendo University School of Medicine.

SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2006 Nov) Vol. 64, No. 11, pp. 2107-12. Ref: 16  
Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan

DOCUMENT TYPE: (ENGLISH ABSTRACT)  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200701

ENTRY DATE: Entered STN: 8 Nov 2006

Last Updated on STN: 10 Jan 2007

Entered Medline: 9 Jan 2007

AB Diabetic macroangiopathy has already developed before diagnosis of diabetes mellitus. Postprandial hyperglycemia has been known as a risk factor for diabetic macroangiopathy and may be more powerful than fasting hyperglycemia. To intervene in hyperglycemia, insulin secretagogues, glinides which selectively stimulate early meal-induced insulin secretion and improve postprandial hyperglycemia, and sulfonylureas which enhance total daily insulin secretion and improve fasting hyperglycemia, have been prescribed as major oral antidiabetic agents. Few evidences that amelioration of glycemic control with insulin secretagogues lower the risk of cardiovascular diseases have been reported. But current studies have shown that intervention in postprandial hyperglycemia with drugs including glinides decreased thickness of carotid IMT as a surrogate marker of atherosclerosis. Results from on-going large scale intervention study with glinides may clarify whether amelioration of hyperglycemia lower the risk of atherosclerotic events.

CT Arteriosclerosis: ET, etiology

\*Arteriosclerosis: PC, prevention & control

Cardiovascular Diseases: ET, etiology

\*Cardiovascular Diseases: PC, prevention & control

\*Cyclohexanes: TU, therapeutic use

Diabetic Angiopathies: ET, etiology

\*Diabetic Angiopathies: PC, prevention & control

Glucose Intolerance: CO, complications

Glucose Intolerance: DT, drug therapy

Hyperglycemia: CO, complications

\*Hyperglycemia: DT, drug therapy

Hyperglycemia: PP, physiopathology

\*Hypoglycemic Agents: TU, therapeutic use

\*Indoles: TU, therapeutic use

Insulin: SE, secretion

\*Phenylalanine: AA, analogs & derivatives

Phenylalanine: TU, therapeutic use

Postprandial Period

Risk Factors

\*Sulfonylurea Compounds: TU, therapeutic use

RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 63-91-2 (Phenylalanine)

CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Sulfonylurea Compounds); 0 (mitiglinide)

L61 ANSWER 30 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2005676318 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 16363700

TITLE: Significance of insulin secretion pattern lectured by  
"glinides" in the treatment of **postprandial  
hyperglycemia**.

AUTHOR: Hirose Takahisa

CORPORATE SOURCE: Department of Medicine, Metabolism and Endocrinology,  
Juntendo University School of Medicine.SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2005  
Dec) Vol. 63, No. 12, pp. 2237-44. Ref: 14  
Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan

DOCUMENT TYPE: (ENGLISH ABSTRACT)  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200603

ENTRY DATE: Entered STN: 22 Dec 2005

Last Updated on STN: 11 Mar 2006

Entered Medline: 10 Mar 2006

AB The mechanisms by which **postprandial hyperglycemia** is elicited were discussed through therapies of type 2 diabetes using "glinides". It has been believed that the earliest determinant of progression to type 2 diabetes is a loss of early insulin secretion, a defect which results in **postprandial hyperglycemia** and is often believed to reflect insulin resistance. To prove that, we improved insulin secretion pattern without increase of total amount of insulin secretion using glinide and assessed glucose response. Glinide which selectively enhances early meal-induced insulin secretion improved **postprandial hyperglycemia**, could provide a valuable treatment option in the prevention and treatment of type 2 diabetes.

CT \*Cyclohexanes: TU, therapeutic use

Diabetes Mellitus, Type 2: CO, complications

Eating

Humans

\*Hyperglycemia: DT, drug therapy

Hyperglycemia: ET, etiology

\*Hypoglycemic Agents: TU, therapeutic use

\*Indoles: TU, therapeutic use

\*Insulin: SE, secretion

\*Phenylalanine: AA, analogs &amp; derivatives

Phenylalanine: TU, therapeutic use

RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 63-91-2 (Phenylalanine)

CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 31 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2005147537 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 15779420

TITLE: Effects of **mitiglinide** in treatment of impaired  
glucose tolerance.

AUTHOR: Katahira Hiroshi; Ishida Hitoshi

CORPORATE SOURCE: Third Department of Internal Medicine, Kyorin University  
School of Medicine.SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2005  
Feb) Vol. 63 Suppl 2, pp. 444-50. Ref: 15  
Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan

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DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200506

ENTRY DATE: Entered STN: 23 Mar 2005

Last Updated on STN: 15 Jun 2005

Entered Medline: 14 Jun 2005

CT Adenosine Triphosphate: ME, metabolism  
Animals  
Diabetes Mellitus, Type 2: ET, etiology  
Diabetes Mellitus, Type 2: PC, prevention & control  
Humans  
Hyperglycemia: CO, complications  
\*Hyperglycemia: DT, drug therapy  
Hypoglycemic Agents: PK, pharmacokinetics  
\*Hypoglycemic Agents: PD, pharmacology  
\*Hypoglycemic Agents: TU, therapeutic use  
Indoles: PK, pharmacokinetics  
\*Indoles: PD, pharmacology  
\*Indoles: TU, therapeutic use  
\*Insulin: SE, secretion  
Postprandial Period  
Potassium Channels: DE, drug effects  
Stimulation, Chemical  
RN 11061-68-0 (Insulin); 56-65-5 (Adenosine Triphosphate)  
CN 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Potassium Channels); 0 (mitiglinide)

L61 ANSWER 32 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2005147534 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 15779417

TITLE: Selection of oral antidiabetic drugs.

AUTHOR: Iwamoto Yasuhiko

CORPORATE SOURCE: Diabetes Center, Tokyo Women's Medical University.

SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2005 Feb) Vol. 63 Suppl 2, pp. 428-32. Ref: 9  
Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200506

ENTRY DATE: Entered STN: 23 Mar 2005

Last Updated on STN: 15 Jun 2005

Entered Medline: 14 Jun 2005

CT Acarbose  
Administration, Oral  
Biguanides  
Cardiovascular Diseases: ET, etiology  
Cardiovascular Diseases: PC, prevention & control  
Diabetes Mellitus, Type 2: ET, etiology  
Diabetes Mellitus, Type 2: PC, prevention & control  
Enzyme Inhibitors  
Glucose Intolerance: CO, complications  
Glucose Intolerance: DT, drug therapy  
Humans  
\*Hypoglycemic Agents  
Hypoglycemic Agents: AD, administration & dosage

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Hypoglycemic Agents: AE, adverse effects  
Hypoglycemic Agents: CL, classification  
Hypoglycemic Agents: PD, pharmacology  
Indoles  
Risk  
Sulfonylurea Compounds  
Thiazolidinediones

**alpha-Glucosidases: AI, antagonists & inhibitors**

RN 2295-31-0 (2,4-thiazolidinedione); 56180-94-0 (Acarbose)  
CN 0 (Biguanides); 0 (Enzyme Inhibitors); 0 (Hypoglycemic Agents);  
0 (Indoles); 0 (Sulfonylurea Compounds); 0 (Thiazolidinediones); 0 (mitiglinide); EC 3.2.1.20 (alpha-Glucosidases)

L61 ANSWER 33 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2004624721 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 15561904

TITLE: The impact of ATP-sensitive K<sup>+</sup> channel subtype selectivity of insulin secretagogues for the coronary vasculature and the myocardium.

AUTHOR: Quast Ulrich; Stephan Damian; Bieger Susanne; Russ Ulrich  
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Medical Faculty, University of Tübingen, Wilhelmstrasse. 56, D-72074 Tübingen, Germany.. ulrich.quast@uni-tuebingen.de

SOURCE: Diabetes, (2004 Dec) Vol. 53 Suppl 3, pp. S156-64. Ref: 58  
Journal code: 0372763. ISSN: 0012-1797.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200504

ENTRY DATE: Entered STN: 20 Dec 2004

Last Updated on STN: 15 Apr 2005

Entered Medline: 14 Apr 2005

AB Insulin secretagogues (sulfonylureas and glinides) increase insulin secretion by closing the ATP-sensitive K<sup>+</sup> channel (KATP channel) in the pancreatic beta-cell membrane. KATP channels subserve important functions also in the heart. First, KATP channels in coronary myocytes contribute to the control of coronary blood flow at rest and in hypoxia. Second, KATP channels in the sarcolemma of cardiomyocytes (sarcoKATP channels) are required for adaptation of the heart to stress. In addition, the opening of sarcoKATP channels and of KATP channels in the inner membrane of mitochondria (mitoKATP channels) plays a central role in ischemic preconditioning. Opening of sarcoKATP channels also underlies the ST-segment elevation of the electrocardiogram, the primary diagnostic tool for initiation of lysis therapy in acute myocardial infarction. Therefore, inhibition of cardiovascular KATP channels by insulin secretagogues is considered to increase cardiovascular risk. Electrophysiological experiments have shown that the secretagogues differ in their selectivity for the pancreatic over the cardiovascular KATP channels, being either highly selective (approximately 1,000x; short sulfonylureas such as nateglinide and mitiglinide), moderately selective (10-20x; long sulfonylureas such as glibenclamide [glyburide]), or essentially nonselective (<2x; repaglinide). New binding studies presented here give broadly similar results. In clinical studies, these differences are not yet taken into account. The hypothesis that the in vitro selectivity of the insulin secretagogues is of importance for the cardiovascular outcome of diabetic patients with coronary artery disease needs to be tested.

CT \*Adenosine Triphosphate: PH, physiology  
Animals

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\*Coronary Circulation: PH, physiology

\*Heart: PH, physiology

Humans

\*Hypoglycemic Agents: PD, pharmacology

\*Insulin: SE, secretion

Models, Molecular

Potassium Channels, Inwardly Rectifying: CH, chemistry

Potassium Channels, Inwardly Rectifying: DE, drug effects

\*Potassium Channels, Inwardly Rectifying: PH, physiology

Protein Conformation

Protein Subunits: CH, chemistry

Sulfonylurea Compounds: PD, pharmacology

RN 11061-68-0 (Insulin); 56-65-5 (Adenosine Triphosphate)

CN 0 (Hypoglycemic Agents); 0 (Kir6.2 channel); 0 (Potassium Channels, Inwardly Rectifying); 0 (Protein Subunits); 0 (Sulfonylurea Compounds)

L61 ANSWER 34 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2004390172 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 15293870

TITLE: Mitiglinide: KAD 1229, S 21403.

AUTHOR: Anonymous

SOURCE: Drugs in R&D, (2004) Vol. 5, No. 2, pp. 98-101. Ref: 13

Journal code: 100883647. ISSN: 1174-5886.

PUB. COUNTRY: New Zealand

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200502

ENTRY DATE: Entered STN: 6 Aug 2004

Last Updated on STN: 4 Feb 2005

Entered Medline: 3 Feb 2005

AB Mitiglinide [KAD 1229, S 21403], a derivative of benzylsuccinic acid, is a potassium channel antagonist undergoing development with Kissei for the treatment of type 2 diabetes mellitus. It has potent oral hypoglycaemic activity and is structurally different from the sulphonylureas, although it stimulates calcium influx by binding to the suphonylurea receptor on pancreatic beta-cells and closing K+ATP channels. Mitiglinide belongs to a family of meglitinide analogues that also includes repaglinide and nateglinide. Mitiglinide is licensed to Servier for Europe, where it is undergoing phase III development, and for Russia, the Commonwealth of Independent States, the Baltic Republics, the Middle East, Oceania, China (including Hong Kong) and Taiwan. Kissei exclusively licensed mitiglinide to Choongwae Pharma for South Korea in March 2003. In August 2002, Kissei and Takeda entered into a co-marketing agreement for mitiglinide in Japan. The companies will co-market the agent under a single brand name. Mitiglinide was licensed to Purdue Pharma for the US, Canada, Mexico and Central and South America. However, Kissei and Purdue Pharma terminated their agreement in February 2001 following Purdue Pharma's decision to concentrate on core areas such as oncology and analgesics. Kissei's US subsidiary, Kissei Pharma US, is currently carrying on the ongoing phase II clinical development in the US. However, in its Annual Report 2003, Kissei announced that it is considering outlicensing mitiglinide for development in marketing in North America. Mitiglinide has been recommended for approval in Japan for the management of postprandial hyperglycaemia in patients with type 2 diabetes. Kissei is also conducting phase II/III clinical trials with a combination of mitiglinide and an alpha-glucosidase inhibitor (additional indication) in patients with type 2 diabetes in Japan. In the US, the agent is being evaluated in phase II clinical trials with Kissei Pharma USA. Mitiglinide is also undergoing a phase-III, 12-month, multicentre, randomised, double-blind study in a total of

710 patients in comparison with repaglinide for the treatment of type 2 diabetes. This study will be followed by a 12-month open-label treatment with mitiglinide alone or in combination therapy. Servier (Australia) conducted a randomised, double-blind, multicentre phase III study in Australia comparing mitiglinide with metformin or a combination of the two for the treatment of type 2 diabetes.

CT Animals

Diabetes Mellitus, Type 2: DT, drug therapy

Humans

Hypoglycemic Agents: PD, pharmacology

\*Hypoglycemic Agents: TU, therapeutic use

Indoles: PD, pharmacology

\*Indoles: TU, therapeutic use

Randomized Controlled Trials

CN 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 35 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2003345780 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12877090

TITLE: Nateglinide and mitiglinide.

AUTHOR: Odawara Masato

CORPORATE SOURCE: Department of Endocrinology and Metabolism, Toranomon Hospital.

SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2003 Jul) Vol. 61, No. 7, pp. 1230-7. Ref: 12  
Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan

DOCUMENT TYPE: (ENGLISH ABSTRACT)

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200309

ENTRY DATE: Entered STN: 25 Jul 2003

Last Updated on STN: 26 Sep 2003

Entered Medline: 25 Sep 2003

AB Patients with type 2 diabetes mellitus are associated with insulin resistance and/or impaired insulin secretion. Previous observations indicate that Japanese patients with type 2 diabetes tend to have impaired insulin response after glycemic load more often than Caucasian counterparts. Recently it has been reported that hyperglycemia after glucose load is itself a risk factor for the development of cardiovascular complications in the absence of elevated fasting plasma glucose. Recent observations on the association of post-challenge or post-prandial hyperglycemia with cardiovascular events suggest that lowering post-prandial plasma glucose may protect patients from developing cardiovascular diseases. Results of STOP-NIDDM trial suggest that nateglinide, which attenuates post-prandial glycemic surge in type 2 diabetes, may also be helpful for the protection against cardiovascular events. Nateglinide exerts its effects shortly after its administration and the effects continue for only about 3 hours. The patients receiving this agent rarely gain weight and develop hypoglycemia. This agent exerts hypoglycemic effects additively with alpha-glucosidase inhibitors or metformin.

CT Cardiovascular Diseases: ET, etiology

Cardiovascular Diseases: PC, prevention & control

Cyclohexanes: PD, pharmacology

\*Cyclohexanes: TU, therapeutic use

Diabetes Mellitus, Type 2: CO, complications

Diabetes Mellitus, Type 2: DT, drug therapy

Drug Therapy, Combination

Humans

Hyperglycemia: CO, complications

\*Hyperglycemia: DT, drug therapy

\*Hypoglycemic Agents: TU, therapeutic use

Indoles: PD, pharmacology

\*Indoles: TU, therapeutic use

\*Insulin: SE, secretion

Insulin Resistance

Metformin: TU, therapeutic use

Phenylalanine: AA, analogs & derivatives

Phenylalanine: PD, pharmacology

\*Phenylalanine: TU, therapeutic use

Postprandial Period

Stimulation, Chemical

RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 63-91-2 (Phenylalanine);  
657-24-9 (Metformin)

CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 36 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2002028119 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11472274

TITLE: Rapid acting insulintropic agents: restoration of early insulin secretion as a physiologic approach to improve glucose control.

AUTHOR: Pratley R E; Foley J E; Dunning B E

CORPORATE SOURCE: Novartis Pharmaceuticals Corporation, 59 Route 10, East Hanover, New Jersey 07936, USA..  
richard.pratley@pharma.novartis.com

SOURCE: Current pharmaceutical design, (2001 Sep) Vol. 7, No. 14, pp. 1375-97. Ref: 143  
Journal code: 9602487. ISSN: 1381-6128.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200112

ENTRY DATE: Entered STN: 21 Jan 2002

Last Updated on STN: 21 Jan 2002

Entered Medline: 4 Dec 2001

AB The loss of early insulin secretion appears to be a critical event in the deterioration in glucose tolerance during the development of type 2 diabetes. There is therefore a strong rationale for developing new antidiabetic agents aimed at restoring or replacing early prandial insulin secretion and thereby curbing mealtime glucose excursions in patients with type 2 diabetes. Four such new agents are either now available (repaglinide and nateglinide) or in clinical development (KAD-1229 and BTS 67 582). Preclinical studies suggest that each of these new insulintropic agents share a common receptor/effector mechanism with the sulfonylureas (SUs) but that each may have distinct characteristics that differentiate them from the SUs and from each other. Nateglinide and KAD-1229 clearly stimulate biphasic insulin secretion in vitro and in vivo and their effects are rapidly reversible, whereas the effects of repaglinide and BTS 67 582 are prolonged well beyond their removal from perfusion media in vitro or their clearance in vivo. Available data from human studies indicate that the pharmacokinetics of repaglinide and nateglinide are similar, i.e., they are both rapidly absorbed and eliminated, but consistent with findings from animal studies, the insulintropic and glucose-lowering effects of repaglinide are slower in onset and more prolonged than those of nateglinide. Repaglinide and nateglinide have been shown to be safe and well-tolerated in patients with type 2 diabetes and to produce

clinically-meaningful reductions of HbA1c, both alone and in combination with agents with complementary modes of action (e.g., metformin and thiazolidinediones). Because these new agents can potentially bring patients to near normoglycemia without an undue risk of hypoglycemia, they are important additions to the therapeutic armamentarium.

## CT Animals

Carbamates: CH, chemistry  
 Carbamates: PK, pharmacokinetics  
 Carbamates: TU, therapeutic use  
 Cyclohexanes: CH, chemistry  
 Cyclohexanes: PK, pharmacokinetics  
 Cyclohexanes: TU, therapeutic use  
 \*Diabetes Mellitus, Type 2: BL, blood  
 \*Diabetes Mellitus, Type 2: DT, drug therapy

\*Glucose: ME, metabolism

Guanidines: CH, chemistry  
 Guanidines: PK, pharmacokinetics  
 Guanidines: TU, therapeutic use

## Humans

Hypoglycemic Agents: CH, chemistry  
 Hypoglycemic Agents: PK, pharmacokinetics  
 \*Hypoglycemic Agents: TU, therapeutic use

Indoles: CH, chemistry  
 Indoles: PK, pharmacokinetics  
 Indoles: TU, therapeutic use  
 Insulin: BL, blood  
 Insulin: PH, physiology

\*Insulin: SE, secretion

\*Phenylalanine: AA, analogs & derivatives

Phenylalanine: CH, chemistry  
 Phenylalanine: PK, pharmacokinetics  
 Phenylalanine: TU, therapeutic use  
 Piperidines: CH, chemistry  
 Piperidines: PK, pharmacokinetics  
 Piperidines: TU, therapeutic use

RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 135062-02-1 (repaglinide); 50-99-7 (Glucose); 63-91-2 (Phenylalanine)

CN 0 (BTS 67582); 0 (Carbamates); 0 (Cyclohexanes); 0 (Guanidines); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Piperidines); 0 (mitiglinide)

L61 ANSWER 37 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2001301378 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11174074

TITLE: Effect of KAD-1229, a nonsulfonylurea hypoglycemic agent, on plasma glucose and insulin in streptozotocin-induced diabetic dogs.

AUTHOR: Misawa K; Ichikawa K; Ojima K; Hamano S; Kitamura T; Komatsu H

CORPORATE SOURCE: Pharmacological Laboratories, Kissei Pharmaceutical Co. Ltd., Hotaka, Nagano, Japan.. keiko\_misawa@pharm.kissei.co.jp

SOURCE: Pharmacology, (2001 Feb) Vol. 62, No. 2, pp. 65-72.

Journal code: 0152016. ISSN: 0031-7012.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200105



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ENTRY DATE: Entered STN: 4 Jun 2001  
Last Updated on STN: 4 Jun 2001  
Entered Medline: 31 May 2001

AB Hypoglycemic agents with a rapid onset and short duration of action should be useful for controlling postprandial hyperglycemia. Our aim was to establish a diabetes mellitus model in dogs, and then during an oral glucose tolerance test to compare the hypoglycemic effect and insulintropic action of KAD-1229, a new hypoglycemic agent, with that of gliclazide, a conventional sulfonylurea. In this model, KAD-1229 reduced the increase in plasma glucose level without producing hypoglycemia. Gliclazide had a weaker effect on reduction of the glucose increase and caused hypoglycemia via a significantly raised insulin secretion in the late phase. A rapid insulintropic action of KAD-1229 was clearly observed in the portal venous blood. The results suggest that in type 2 diabetes caused by, at least, insulin deficiency, KAD-1229 may improve impaired insulin secretion in the early phase and attenuate hyperglycemia without causing a sustained hypoglycemia. Copyright 2001 S. Karger AG, Basel.

CT Check Tags: Male  
Animals  
Anti-Bacterial Agents  
\*Blood Glucose: DE, drug effects  
\*Diabetes Mellitus, Experimental: BL, blood  
Disease Models, Animal  
Dogs  
Gliclazide: PD, pharmacology  
Glucose Tolerance Test  
\*Hypoglycemic Agents: PD, pharmacology  
\*Indoles: PD, pharmacology  
\*Insulin: BL, blood  
Streptozocin

RN 11061-68-0 (Insulin); 18883-66-4 (Streptozocin); 21187-98-4 (Gliclazide)  
CN 0 (Anti-Bacterial Agents); 0 (Blood Glucose); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 38 OF 49 MEDLINE on STN

ACCESSION NUMBER: 1999215370 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10199157

TITLE: Non-SU, insulin secretagogues.

AUTHOR: Kikuchi M

CORPORATE SOURCE: Institute for Adult Diseases, Asahi Life Foundation.

SOURCE: Nippon rinsho. Japanese journal of clinical medicine,  
(1999 Mar) Vol. 57, No. 3, pp. 702-8. Ref: 21  
Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan

DOCUMENT TYPE: (ENGLISH ABSTRACT)

Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199905

ENTRY DATE: Entered STN: 1 Jun 1999

Last Updated on STN: 1 Jun 1999

Entered Medline: 18 May 1999

AB The chemical structures, mechanisms of actions, bioavailabilities, insulintrophic and hypoglycemic actions, and clinical trials of three novel oral hypoglycemic agents, NN-623, A-4166 and KAD-1229 are overviewed. They are non-SU insulin secretagogues and they induce quicker and shorter hypoglycemia than sulphonylureas do, presumably because they are rapidly absorbed into (Tmax: < 30 min) and excreted from blood (T 1/2: < 60 min). They bind to the SU-receptors and suppress K-ATP channels like sulphonylureas

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do. They stimulate mainly the initial phase of insulin release and evoke a decrease in postprandial rises in plasma glucose in several animals and humans. Clinical trials demonstrated they are efficacious and safe in the treatment of NIDDM subjects. They are useful as a first choice drug for the early stage of NIDDM.

CT \*Cyclohexanes: TU, therapeutic use

\*Diabetes Mellitus, Type 2: DT, drug therapy

Humans

\*Hypoglycemic Agents: TU, therapeutic use

\*Indoles: TU, therapeutic use

\*Phenylalanine: AA, analogs & derivatives

Phenylalanine: TU, therapeutic use

RN 105816-04-4 (nateglinide); 63-91-2 (Phenylalanine)

CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 39 OF 49 MEDLINE on STN

ACCESSION NUMBER: 1999410611 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10479476

TITLE: Effect of the meglitinide analog S21403 on cationic fluxes and insulin release in perfused rat pancreatic islets exposed to a high concentration of D-glucose.

AUTHOR: Louchami K; Jijakli H; Malaisse W J

CORPORATE SOURCE: Laboratory of Experimental Medicine, Brussels Free University, 808 Route de Lennik, Brussels, B-1070, Belgium.

SOURCE: Pharmacological research : the official journal of the Italian Pharmacological Society, (1999 Sep) Vol. 40, No. 3, pp. 297-300.

Journal code: 8907422. ISSN: 1043-6618.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199911

ENTRY DATE: Entered STN: 11 Jan 2000

Last Updated on STN: 11 Jan 2000

Entered Medline: 1 Nov 1999

AB The effect of the meglitinide analog S21403 (10 microm) upon (86)Rb and (45)Ca outflow and insulin release was investigated in perfused rat islets exposed to a high concentration of D-glucose (16.7 mM) in order to simulate the situation found in diabetic patients. Under these conditions, S21403 provoked a rapid, sustained and rapidly reversible increase in (86)Rb outflow, (45)Ca efflux and insulin release. These effects were suppressed or reversed when the experiments were conducted in the absence of extracellular Ca<sup>2+</sup>. They support the view that S21043 could be used as a novel insulinotropic tool in the treatment of non-insulin-dependent diabetes mellitus, the cationic and secretory responses to the drug displaying a favourable time course for prompt and not unduly prolonged activation of islet B-cells. Copyright 1999 Academic Press.

CT Check Tags: Female

Animals

Calcium: ME, metabolism

\*Calcium: PK, pharmacokinetics

Calcium Radioisotopes

Cations

\*Glucose: PD, pharmacology

\*Hypoglycemic Agents: PD, pharmacology

\*Indoles: PD, pharmacology

\*Insulin: SE, secretion

\*Islets of Langerhans: DE, drug effects

\*Islets of Langerhans: ME, metabolism

Islets of Langerhans: SE, secretion  
Perfusion

Rats

Rats, Wistar

\*Rubidium: PK, pharmacokinetics

Rubidium Radioisotopes

RN 11061-68-0 (Insulin); 50-99-7 (Glucose); 7440-17-7 (Rubidium); 7440-70-2 (Calcium)

CN 0 (Calcium Radioisotopes); 0 (Cations); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Rubidium Radioisotopes); 0 (mitiglinide)

L61 ANSWER 40 OF 49

MEDLINE on STN

ACCESSION NUMBER: 2000280282 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10820647

TITLE: Recent developments and emerging therapies for type 2 diabetes mellitus.

AUTHOR: Evans A J; Krentz A J

CORPORATE SOURCE: Department of Diabetes and Endocrinology, Southampton General Hospital, England.

SOURCE: Drugs in R&D, (1999 Aug) Vol. 2, No. 2, pp. 75-94. Ref: 106

Journal code: 100883647. ISSN: 1174-5886.

PUB. COUNTRY: New Zealand

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200008

ENTRY DATE: Entered STN: 11 Aug 2000

Last Updated on STN: 11 Aug 2000

Entered Medline: 1 Aug 2000

AB Most patients with type 2 (non-insulin-dependent) diabetes mellitus require pharmacotherapy, initially as monotherapy and subsequently in combination, as adjuncts to diet and exercise. Exogenous insulin is ultimately required in a substantial proportion, reflecting the progressive natural history of the disease. Sulphonylureas and biguanides have been employed for over 4 decades as oral antidiabetic agents, but they have a limited capacity to provide long term glycaemic control and can cause serious adverse effects. Thus, more efficacious and tolerable antidiabetic agents are required. Recent years have witnessed the introduction of agents with novel modes of action, that is, the alpha-glucosidase inhibitors acarbose and miglitol (which reduce postprandial hyperglycaemia) and the first of the thiazolidinedione insulinsensitising drugs--troglitazone and rosiglitazone. Although the former has been withdrawn in some countries due to adverse effects, another 'glitazone' pioglitazone is expected to be approved in the near future. Other recently introduced drugs include glimepiride and the meglitinide insulin secretagogue, repaglinide. Attention is also focusing increasingly on combination therapy using insulin together with sulphonylureas, metformin or troglitazone. Rapid-acting insulin analogues are now being used as alternatives to conventional insulins; their role in the management of type 2 diabetes mellitus is presently uncertain but reports of a reduced frequency of hypoglycaemia are encouraging. The development of new drugs aims to counter the principal metabolic defects of the disorder, respectively, relative insulin deficiency and insulin resistance. Novel classes of rapid-acting secretagogues under evaluation include the morpholinoguanide BTS 67582 and the meglitinides mitiglinide (KAD 1229) and senaglinide (A-4166). Succinate ester derivatives represent a potential novel approach to improving beta-cell function through enhancement of insulin biosynthesis and secretion. Enhancement of nutrient-induced insulin

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secretion is a mechanism with several putative targets within the beta-cell; potentiators of insulin secretion include glucagon-like peptide-1 and its analogues, phosphodiesterase inhibitors and the imidazoline derivative PMS 812 (S 21663). The amylin agonist pramlintide slows gastric emptying and suppression of glucagon secretion. Non-thiazolidinedione insulin-sensitising agents include the gamma-receptor agonist G 1262570X (GG 570) and D-chiro-inositol. Insulin analogues with prolonged action and inhaled insulin preparations are also under investigation. Insulin-mimetic agents include organic vanadium compounds. Whether newer agents will offer clinically relevant efficacy and tolerability advantages over existing therapies remains to be determined.

CT Diabetes Mellitus, Type 2: DH, diet therapy  
\*Diabetes Mellitus, Type 2: DT, drug therapy

Humans

Hypoglycemic Agents: AE, adverse effects

Hypoglycemic Agents: CL, classification

Hypoglycemic Agents: PD, pharmacology

\*Hypoglycemic Agents: TU, therapeutic use

CN 0 (Hypoglycemic Agents)

L61 ANSWER 41 OF 49 MEDLINE on STN

ACCESSION NUMBER: 97041658 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 8886929

TITLE: A rapid- and short-acting hypoglycemic agent KAD-1229 improves post-prandial hyperglycemia and diabetic complications in streptozotocin-induced non-insulin-dependent diabetes mellitus rats.

AUTHOR: Ohnota H; Kitamura T; Kinukawa M; Hamano S; Shibata N; Miyata H; Ujiie A

CORPORATE SOURCE: Central Research Laboratories, Kissei Pharmaceutical Co., Ltd., Nagano, Japan.

SOURCE: Japanese journal of pharmacology, (1996 Aug) Vol. 71, No. 4, pp. 315-23.  
Journal code: 2983305R. ISSN: 0021-5198.

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199701

ENTRY DATE: Entered STN: 19 Feb 1997

Last Updated on STN: 19 Feb 1997

Entered Medline: 30 Jan 1997

AB We investigated therapeutic effects of a rapid- and short-acting non-sulfonylurea hypoglycemic agent, calcium (2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinylicarbonyl)propionate dihydrate (KAD-1229), on streptozotocin (STZ)-induced non-insulin-dependent diabetes mellitus (NIDDM) rats. The effects exerted by KAD-1229 on the post-prandial plasma glucose rise in STZ-induced mild NIDDM (mNIDDM) rats were different from those of sulfonylureas. When KAD-1229 with liquid meal (10 kcal/kg) was given to the mNIDDM rats, the plasma glucose migration was similar to that of normal healthy rats. On the contrary, glibenclamide had little or no effect on the plasma glucose rise 0.5-1 hr after oral administration, and its effect was only evident 2-5 hr after dosing. Tolbutamide showed similar hypoglycemia to that induced by glibenclamide at 2-5 hr with insufficient efficacy at 0.5 hr. Gliclazide sufficiently suppressed the level of post-prandial plasma glucose. However, its complete inhibition of post-prandial plasma glucose was associated with the extra-hypoglycemia 1-5 hr after oral administration. We also tested the efficacy of KAD-1229 in more severe STZ-induced NIDDM (sNIDDM) rats to elucidate the effects of the drug on the long-term glycemic controls and

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diabetic complications. When the SNIDDM rats were treated with 10 mg/kg KAD-1229 twice a day for about 17 weeks, increases in fasting plasma glucose and hemoglobin A1c were inhibited. Furthermore, treatment with KAD-1229 suppressed the development of microalbuminuria and cortical cataract. We conclude that the rapid- and short-acting insulinotropic agent KAD-1229 is able to improve the deterioration in the glycemic controls and inhibit the development of diabetic complications in STZ-induced NIDDM rats.

CT Check Tags: Male

Albuminuria: ME, metabolism

Analysis of Variance

Animals

Blood Glucose: ME, metabolism

Diabetes Mellitus, Experimental: BL, blood

\*Diabetes Mellitus, Experimental: DT, drug therapy

Glucagon: BL, blood

Hyperglycemia: DT, drug therapy

\*Hypoglycemic Agents: PD, pharmacology

\*Indoles: PD, pharmacology

Insulin: BL, blood

Pancreas: CH, chemistry

Pancreas: EN, enzymology

Rats

Rats, Sprague-Dawley

Streptozocin

RN 11061-68-0 (Insulin); 18883-66-4 (Streptozocin); 9007-92-5 (Glucagon)

CN 0 (Blood Glucose); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 42 OF 49

MEDLINE on STN

ACCESSION NUMBER: 95323823 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 7600439

TITLE: Normalization of impaired glucose tolerance by the short-acting hypoglycemic agent calcium (2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinylicarbonyl)propionate dihydrate (KAD-1229) in non-insulin-dependent diabetes mellitus rats.

AUTHOR: Ohnota H; Koizumi T; Kobayashi M; Momose Y; Sato F

CORPORATE SOURCE: Creative Products Research Laboratory, Kissei Pharmaceutical Co., Ltd., Nagano-ken, Japan.

SOURCE: Canadian journal of physiology and pharmacology, (1995 Jan) Vol. 73, No. 1, pp. 1-6.

Journal code: 0372712. ISSN: 0008-4212.

PUB. COUNTRY: Canada

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199508

ENTRY DATE: Entered STN: 22 Aug 1995

Last Updated on STN: 22 Aug 1995

Entered Medline: 7 Aug 1995

AB We have investigated the hypoglycemic effects of the newly synthesized short-acting nonsulphonylurea hypoglycemic agent calcium (2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinylicarbonyl)-propionate dihydrate (KAD-1229) in non-insulin-dependent diabetes mellitus (NIDDM) rats. NIDDM rats that were given a neonatal injection of 60 mg/kg streptozotocin showed a dose-dependent but attenuated response to oral administration of KAD-1229 and gliclazide, and their impaired glucose tolerance was improved but not normalized. We next produced, using a neonatal injection of 30 mg/kg streptozotocin, a mild type of NIDDM rat with less impaired glucose tolerance. These rats responded well to these insulinotropic hypoglycemic agents. Their impaired glucose and meal

tolerance were completely normalized by oral administration of 3 mg/kg KAD-1229. The efficacy of KAD-1229 in this NIDDM rat model 1-3 h after oral glucose administration was comparable with similar doses of gliclazide, despite its shorter hypoglycemic action (compared with gliclazide), in fasting normal rats. In meal tolerance tests (20 kcal/kg; 1 cal = 4.2 J), KAD-1229 reduced abnormally enhanced plasma glucose levels 1-3 h after administration. This effect disappeared by 5 h. In contrast, gliclazide showed sustained hypoglycemic effects until 5 h after oral administration, with a lower postprandial (0.5-1 h) effect. These data indicated that the rapid- and short-acting efficacy of KAD-1229 would be beneficial and sufficient to control postprandial plasma glucose in NIDDM rats.

CT Animals  
Animals, Newborn  
\*Blood Glucose: ME, metabolism  
\*Diabetes Mellitus, Experimental: BL, blood  
Food  
Gliclazide: PD, pharmacology  
Glucose Tolerance Test  
\*Hypoglycemic Agents: PD, pharmacology  
Immunohistochemistry  
\*Indoles: PD, pharmacology  
Pancreas: ME, metabolism  
Rats  
Rats, Sprague-Dawley  
RN 21187-98-4 (Gliclazide)  
CN 0 (Blood Glucose); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

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ACCESSION NUMBER: 2003324437 EMBASE Full-text  
TITLE: Sulphonylurea action revisited: The post-cloning era.  
AUTHOR: Gribble F.M.; Reimann F.  
CORPORATE SOURCE: Dr. F.M. Gribble, Department of Clinical Biochemistry, Addenbrooke's Hospital, Box 232, Hills Road, Cambridge, CB2 2QR, United Kingdom. fmg23@cam.ac.uk  
SOURCE: Diabetologia, (1 Jul 2003) Vol. 46, No. 7, pp. 875-891. .  
Refs: 163  
ISSN: 0012-186X CODEN: DBTGJ  
COUNTRY: Germany  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 003 Endocrinology  
006 Internal Medicine  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 4 Sep 2003  
Last Updated on STN: 4 Sep 2003

AB Hypoglycaemic agents such as sulphonylureas and the newer group of "glinides" stimulate insulin secretion by closing ATP-sensitive potassium (K(ATP)) channels in pancreatic beta cells, but have varying cross-reactivity with related channels in extrapancreatic tissues such as heart, vascular smooth and skeletal muscle. Experiments on the structure-function relationships of recombinant K(ATP) channels and the phenotypes of mice deficient in different K(ATP) channel subunits have provided important insights into the mechanisms underlying sulphonylurea selectivity, and the potential consequences of K(ATP) channel blockade outside the pancreatic beta cell. The different pharmacological properties of K(ATP) channels from beta cells compared with

those from cardiac, smooth and skeletal muscle, are accounted for by the expression of alternative types of sulphonylurea receptor, with non-identical drug binding sites. The sulphonylureas and glinides are found to fall into two groups: one exhibiting selectivity for beta cell sulphonylurea receptors (SUR1), and the other blocking cardiovascular and skeletal muscle sulphonylurea receptors (SUR2) with potencies similar to their action on SUR1. In seeking potential side effects of K(ATP) channel inhibitors in humans, it is essential to take these drug differences into account, along with the probability (suggested by the studies on K(ATP) channel knockout mice) that the effects of extrapancreatic K(ATP) channel inhibition might be either subtle or rare. Further studies are still required before a final decision can be made on whether non-selective agents are appropriate for the therapy of Type 2 diabetes.

CT Medical Descriptors:

\*non insulin dependent diabetes mellitus: DT, drug therapy  
 drug mechanism  
 drug effect  
 drug receptor binding  
 insulin release  
 inwardly rectifying potassium channel  
 pancreas islet beta cell  
 cross reaction  
 heart  
 vascular smooth muscle  
 skeletal muscle  
 phenotype  
 drug selectivity  
 protein expression  
 drug binding site  
 drug potency  
 side effect: SI, side effect  
 knockout mouse  
 medical decision making  
 cloning  
 human  
 nonhuman  
 review  
 priority journal  
 Drug Descriptors:  
 \*sulfonylurea: AE, adverse drug reaction  
 \*sulfonylurea: IT, drug interaction  
 \*sulfonylurea: DT, drug therapy  
 \*sulfonylurea: PD, pharmacology  
 tolbutamide: DT, drug therapy  
 tolbutamide: PD, pharmacology  
 gliclazide: DT, drug therapy  
 gliclazide: PD, pharmacology  
 mitiglinide: DT, drug therapy  
 mitiglinide: PD, pharmacology  
 glibenclamide: DT, drug therapy  
 glibenclamide: PD, pharmacology  
 glimepiride: DT, drug therapy  
 glimepiride: PD, pharmacology  
 repaglinide: DT, drug therapy  
 repaglinide: PD, pharmacology  
 insulin: EC, endogenous compound  
 adenosine triphosphate  
 sulfonylurea receptor: EC, endogenous compound  
 receptor subtype: EC, endogenous compound  
 chlorpropamide: DT, drug therapy

chlorpropamide: PD, pharmacology  
 meglitinide: DT, drug therapy  
 meglitinide: PD, pharmacology  
 nateglinide: DT, drug therapy  
 nateglinide: PD, pharmacology  
 diazoxide: IT, drug interaction  
 diazoxide: PD, pharmacology  
 nicorandil: DT, drug therapy  
 nicorandil: PD, pharmacology  
 pinacidil  
 cromakalim

RN (tolbutamide) 473-41-6, 64-77-7; (gliclazide) 21187-98-4; (  
 mitiglinide) 145525-41-3, 207844-01-7; (glibenclamide)  
 10238-21-8; (glimepiride) 93479-97-1; (repaglinide) 135062-02-1; (insulin)  
 9004-10-8; (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5;  
 (chlorpropamide) 94-20-2; (meglitinide) 54870-28-9; (nateglinide)  
 105746-37-0, 105816-04-4, 105816-06-6; (diazoxide) 364-98-7; (nicorandil)  
 65141-46-0; (pinacidil) 60560-33-0; (cromakalim) 94470-67-4

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ACCESSION NUMBER: 2003422728 EMBASE Full-text

TITLE: [Current oral agents for type 2 diabetes].  
 TIP 2 DIYABETTE GUNCEL ORAL AJANLAR.

AUTHOR: Stoller W.A.

SOURCE: SENDROM, (2003) Vol. 15, No. 6, pp. 24-33. .  
 Refs: 22

ISSN: 1016-5134 CODEN: SENDEY

COUNTRY: Turkey

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 003 Endocrinology  
 017 Public Health, Social Medicine and Epidemiology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles

LANGUAGE: Turkish

SUMMARY LANGUAGE: English; Turkish

ENTRY DATE: Entered STN: 6 Nov 2003

Last Updated on STN: 6 Nov 2003

AB Type 2 diabetes has reached epidemic levels in the United States. Progressive  
 evidence has emphasized the importance of glucose control in avoiding the high  
 costs and reduced quality of life associated with the numerous complications  
 of diabetes. Fortunately, pharmacologic options for treating type 2 diabetes  
 have increased dramatically during the last 6 years, allowing new  
 opportunities for successful outcomes. Such options will continue to expand.  
 Therefore we are challenged to effectively use these agents in a logical  
 progressive regimen while minimizing side effects.

CT Medical Descriptors:

\*non insulin dependent diabetes mellitus: DT, drug therapy

\*non insulin dependent diabetes mellitus: EP, epidemiology

United States

quality of life

cost of illness

pathophysiology

hypoglycemia: SI, side effect

meteorism: SI, side effect

anorexia: SI, side effect

side effect: SI, side effect

human

review

Drug Descriptors:



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\*oral antidiabetic agent: AE, adverse drug reaction  
\*oral antidiabetic agent: DT, drug therapy  
\*oral antidiabetic agent: PO, oral drug administration  
sulfonylurea: AE, adverse drug reaction  
sulfonylurea: DT, drug therapy  
sulfonylurea: PO, oral drug administration  
glibenclamide: DT, drug therapy  
glibenclamide: PO, oral drug administration  
glimepiride: DT, drug therapy  
glimepiride: PO, oral drug administration  
glipizide: DT, drug therapy  
glipizide: PO, oral drug administration  
repaglinide: AE, adverse drug reaction  
repaglinide: DT, drug therapy  
repaglinide: PO, oral drug administration  
  mitiglinide: DT, drug therapy  
  mitiglinide: PO, oral drug administration  
nateglinide: AE, adverse drug reaction  
nateglinide: DT, drug therapy  
nateglinide: PO, oral drug administration  
  alpha glucosidase inhibitor: DT, drug therapy  
  alpha glucosidase inhibitor: PO, oral drug administration  
metformin: AE, adverse drug reaction  
metformin: DT, drug therapy  
metformin: PO, oral drug administration  
insulin: DT, drug therapy  
peroxisome proliferator activated receptor agonist: AE, adverse drug reaction  
peroxisome proliferator activated receptor agonist: DT, drug therapy  
peroxisome proliferator activated receptor agonist: PO, oral drug administration  
pioglitazone: DT, drug therapy  
pioglitazone: PO, oral drug administration  
rosiglitazone: DT, drug therapy  
rosiglitazone: PO, oral drug administration  
human insulin: DT, drug therapy  
insulin glargine: DT, drug therapy  
hemoglobin Alc: EC, endogenous compound  
acarbose: AE, adverse drug reaction  
acarbose: DT, drug therapy  
acarbose: PO, oral drug administration  
miglitol: AE, adverse drug reaction  
miglitol: DT, drug therapy  
miglitol: PO, oral drug administration  
glibenclamide plus metformin  
starfix

RN (glibenclamide) 10238-21-8; (glimepiride) 93479-97-1; (glipizide) 29094-61-9; (repaglinide) 135062-02-1; (mitiglinide) 145525-41-3, 207844-01-7; (nateglinide) 105746-37-0, 105816-04-4, 105816-06-6; (metformin) 1115-70-4, 657-24-9; (insulin) 9004-10-8; (pioglitazone) 105355-27-9, 111025-46-8; (rosiglitazone) 122320-73-4, 155141-29-0; (human insulin) 11061-68-0; (insulin glargine) 160337-95-1; (hemoglobin Alc) 62572-11-6; (acarbose) 56180-94-0; (miglitol) 72432-03-2

CN Humulin; Novolin; Lantus; Glucovance; Prandin; Starfix; Precose; Glyset

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ACCESSION NUMBER: 2004050138 EMBASE Full-text

TITLE: World Congress of Pharmacology - XIVth Annual Meeting: New

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drugs I: 7-12 July 2002, San Francisco, CA, USA.  
AUTHOR: Waterworth C.; Durrance A.  
CORPORATE SOURCE: C. Waterworth, Current Drugs Ltd., Middlesex House, 34-42  
Cleveland Street, London W1T 4LB, United Kingdom.  
charlotte.waterworth@current.drugs.com  
SOURCE: IDrugs, (2002) Vol. 5, No. 8, pp. 745-748. .  
ISSN: 1369-7056 CODEN: IDRUFN  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 037 Drug Literature Index  
029 Clinical Biochemistry  
025 Hematology  
030 Pharmacology  
018 Cardiovascular Diseases and Cardiovascular Surgery  
LANGUAGE: English  
ENTRY DATE: Entered STN: 12 Feb 2004  
Last Updated on STN: 12 Feb 2004

CT Medical Descriptors:  
human  
clinical trial  
nonhuman  
protein targeting  
thrombocyte aggregation  
kidney function  
diabetes mellitus  
Alzheimer disease  
drug potency  
drug activity  
drug structure  
drug dose regimen  
thrombosis: DT, drug therapy  
atherosclerosis: DT, drug therapy  
drug effect  
obesity: DT, drug therapy  
dose response  
area under the curve  
cognitive defect: DT, drug therapy  
drug metabolism  
drug half life  
drug bioavailability  
drug blood level  
glaucoma: DT, drug therapy  
tumor: DT, drug therapy  
conference paper

CT Drug Descriptors:  
\*new drug: PD, pharmacology  
\*new drug: AN, drug analysis  
\*new drug: DO, drug dose  
\*new drug: CM, drug comparison  
\*new drug: DT, drug therapy  
\*new drug: PO, oral drug administration  
\*new drug: CT, clinical trial  
\*new drug: PK, pharmacokinetics  
\*new drug: CR, drug concentration  
purine P2Y receptor: EC, endogenous compound  
antithrombocytic agent: PD, pharmacology  
antithrombocytic agent: AN, drug analysis  
antithrombocytic agent: DO, drug dose  
antithrombocytic agent: CM, drug comparison  
antithrombocytic agent: DT, drug therapy

dinucleoside polyphosphate inhibitor: PD, pharmacology  
 dinucleoside polyphosphate inhibitor: AN, drug analysis  
 dinucleoside polyphosphate inhibitor: DO, drug dose  
 dinucleoside polyphosphate inhibitor: CM, drug comparison  
 dinucleoside polyphosphate inhibitor: DT, drug therapy  
 peroxisome proliferator activated receptor agonist: DT, drug therapy  
 peroxisome proliferator activated receptor agonist: PD, pharmacology  
 peroxisome proliferator activated receptor agonist: CM, drug comparison  
 peroxisome proliferator activated receptor agonist: AN, drug analysis  
 acetylsalicylic acid 3 (nitroxymethyl)phenyl ester: DT, drug therapy  
 acetylsalicylic acid 3 (nitroxymethyl)phenyl ester: CM, drug comparison  
 acetylsalicylic acid 3 (nitroxymethyl)phenyl ester: PD, pharmacology  
 mitiglinide: DT, drug therapy  
 mitiglinide: PD, pharmacology  
 mitiglinide: PK, pharmacokinetics  
 mitiglinide: DO, drug dose  
 mitiglinide: AN, drug analysis  
 peptide derivative: DT, drug therapy  
 peptide derivative: CT, clinical trial  
 peptide derivative: PD, pharmacology  
 peptide derivative: AN, drug analysis  
 noopept: DT, drug therapy  
 noopept: CT, clinical trial  
 noopept: PD, pharmacology  
 noopept: AN, drug analysis  
 pirfenidone: DT, drug therapy  
 pirfenidone: CT, clinical trial  
 pirfenidone: PK, pharmacokinetics  
 pirfenidone: IV, intravenous drug administration  
 pirfenidone: DO, drug dose  
 pirfenidone: AN, drug analysis  
 nitronaproxen: DT, drug therapy  
 nitronaproxen: PK, pharmacokinetics  
 nitronaproxen: PO, oral drug administration  
 nitronaproxen: CR, drug concentration  
 nitronaproxen: PD, pharmacology  
 nitronaproxen: AN, drug analysis  
 6 chloro 2 [(1 furo[2,3 c]pyridin 5 ylethyl)thio] 4 pyrimidinamine: DT, drug therapy  
 6 chloro 2 [(1 furo[2,3 c]pyridin 5 ylethyl)thio] 4 pyrimidinamine: CT, clinical trial  
 6 chloro 2 [(1 furo[2,3 c]pyridin 5 ylethyl)thio] 4 pyrimidinamine: AN, drug analysis  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DO, drug dose  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PK, pharmacokinetics  
 antiglaucoma agent: DT, drug therapy  
 antiglaucoma agent: CT, clinical trial  
 antiglaucoma agent: PD, pharmacology  
 antineoplastic agent: DT, drug therapy  
 antineoplastic agent: PD, pharmacology  
 nitrostyrene derivative: DT, drug therapy  
 nitrostyrene derivative: PD, pharmacology

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endothelin converting enzyme inhibitor: DT, drug therapy  
endothelin converting enzyme inhibitor: PD, pharmacology  
cgs 35066: DT, drug therapy  
cgs 35066: PD, pharmacology  
bis (7 tacrine): DT, drug therapy  
bis (7 tacrine): PD, pharmacology  
bis (7 tacrine): AN, drug analysis  
bis (7 tacrine): DO, drug dose  
conivaptan: DT, drug therapy  
conivaptan: PD, pharmacology  
conivaptan: CB, drug combination  
conivaptan: AN, drug analysis  
conivaptan: CM, drug comparison  
conivaptan: DO, drug dose  
carbamic acid derivative: PD, pharmacology  
carbamic acid derivative: AN, drug analysis  
carbamic acid derivative: DO, drug dose  
carbamic acid derivative: CM, drug comparison  
carbamic acid derivative: DT, drug therapy  
diquafosol: PD, pharmacology  
diquafosol: CM, drug comparison  
diquafosol: DT, drug therapy  
ns 220: DT, drug therapy  
ns 220: PD, pharmacology  
ns 220: CM, drug comparison  
ns 220: AN, drug analysis  
fenofibrate: DT, drug therapy  
fenofibrate: PD, pharmacology  
fenofibrate: CM, drug comparison  
acetylsalicylic acid: DT, drug therapy  
acetylsalicylic acid: CM, drug comparison  
acetylsalicylic acid: PD, pharmacology  
a 331440: DT, drug therapy  
a 331440: PO, oral drug administration  
a 331440: DO, drug dose  
a 331440: CM, drug comparison  
a 331440: PD, pharmacology  
dexfenfluramine: DT, drug therapy  
dexfenfluramine: CM, drug comparison  
dexfenfluramine: PD, pharmacology  
thioperamide: DT, drug therapy  
thioperamide: CM, drug comparison  
thioperamide: PD, pharmacology  
ciprofloxacin: DT, drug therapy  
ciprofloxacin: CM, drug comparison  
ciprofloxacin: PD, pharmacology  
unindexed drug  
unclassified drug  
ins 48372  
ins 46116  
ins 46117  
ins 46061  
ins 46058  
ins 48795  
ins 40150  
ins 40270  
ins 46060  
ins 49162  
ins 46059  
s 35836 1

s 35678 1

gvs 111

ot 7999

- RN (acetylsalicylic acid 3 (nitroxymethyl)phenyl ester) 190442-10-5; (mitiglinide) 145525-41-3, 207844-01-7; (pirfenidone) 53179-13-8; (nitronaproxen) 163133-43-5; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (conivaptan) 168626-94-6, 210101-16-9; (diuafosol) 211427-08-6; (fenofibrate) 49562-28-9; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (dexfenfluramine) 3239-44-9, 3239-45-0; (thioparamide) 106243-16-7; (ciprofloxacin) 85721-33-1
- CN (1) Ins 48372; (2) Ins 46116; (3) Ins 46117; (4) Ins 46061; (5) Ins 46058; (6) Ins 48795; (7) Ins 40150; (8) Ins 40270; (9) Ins 46060; (10) Ins 49162; (11) Ins 46059; (12) Ins 365; (13) Ns 220; (14) A 331440; (15) Kad 1229; (16) Kad 1229; (17) S 35836 1; (18) S 35678 1; (19) Kad 1229; (20) Gvs 111; (21) Azd 3582; (22) Azd 3582; (23) Ncx 4016; (24) Pnu 142721; (25) Su 6668; (26) Ot 7999; (27) Cgs 35066; (28) Ym 087; (29) Ym 087; (30) Amr 69; (31) Amr 69; (32) Amr 69; (33) Amr 69
- CO (12) Inspire; (13) Nippon Shinyaku; (14) Abbott; (15) Kissei; (18) Servier; (19) Takeda; (20) Russian Academy of Sciences; (21) Astra Zeneca; (23) Nicox; (24) Pharmacia (United States); (25) Sugen; (26) Otsuka; (27) Novartis; (28) Yamanouchi; (29) Pfizer; (30) Marnac; (31) Intermune; (32) Schering AG; (33) Shionogi; UCB

L61 ANSWER 46 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-08972 DRUGU T S E Full-text

TITLE: Diabetes and insulin resistance associated disorders: disease and the therapy.

AUTHOR: Chakrabarti R; Rajagopalan R

CORPORATE SOURCE: Dr.Reddy's-Lab.

LOCATION: Hyderabad, India

SOURCE: Curr.Sci. (83, No. 12, 1533-38, 2002) 2 Fig. 2 Tab. 18 Ref. CODEN: CUSCAM ISSN: 0011-3891

AVAIL. OF DOC.: Dr. Reddy's Laboratories Ltd., Discovery Research, Bollaram Road, Miyapur, Hyderabad 500 050, India. (R.R.). (e-mail: rajagopalanr@drreddys.com).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The therapy of diabetes and insulin resistance associated disorders are reviewed. Topics covered are classes of currently available drugs and future targets. Established drugs and those in trials discussed are acetohexamide, chlorpropamide, tolbutamide, tolazamide, glyburide, glipizide, glimiperide, repaglinide, nateglinide, glibenclamide, mitiglinide, metformin, phenformin, ciglitazone, troglitazone, rosiglitazone, pioglitazone, acarbose, miglitol (side-effects of these drugs were also mentioned), balaglitazone, natoglitazone, ragaglitazar, tesaglitazar, KRP-297, BMS-298585, regaglitazar, SR-58611, TAK-677, GP-3034, LAF-237, P-32-98, DPP-728 and NN-2211. Current research efforts are focussed on insulin sensitizers, PPAR agonists, protein tyrosine phosphatase inhibitors, beta-3 adrenoceptor agonists, inhibitors of hepatic glucose output and insulin secretagogues. (No EX).

AN 2003-08972 DRUGU T S E Full-text

T Therapeutics

S Adverse Effects

E Endocrinology

12 Antidiabetics

35 Adverse Reactions

64 Clinical Trials

69 Reviews

73 Trial Preparations  
 CT DIABETES \*TR; CARBOHYDRATE-METAB.DISORDER \*TR; PANCREOPATHY  
 \*TR; CASES \*FT; IN-VIVO \*FT; ANTIDIABETIC \*FT; CLIN.TRIAL \*FT; REVIEW  
 \*FT  
 [01] MAIN-TOPIC \*FT; ANTIDIABETICS \*FT; TR \*FT; AE \*FT  
 [02] ACETOHEXAMIDE \*TR; CHLORPROPAMIDE \*TR; TOLBUTAMIDE \*TR; TOLAZAMIDE  
 \*TR; GLIBENCLAMIDE \*TR; GLIPIZIDE \*TR; GLIMIPERIDE \*TR; REPAGLINIDE  
 \*TR; NATEGLINIDE \*TR; GLIBENCLAMIDE \*TR; MITIGLINIDE \*TR;  
 METFORMIN \*TR; PHENFORMIN \*TR; CIGLITAZONE \*TR; TROGLITAZONE \*TR;  
 ROSIGLITAZONE \*TR; PIOGLITAZONE \*TR; ACARBOSE \*TR; MIGLITOL \*TR;  
 BALAGLITAZONE \*TR; NATOGLITAZONE \*TR; RAGAGLITAZAR \*TR; TESAGLITAZAR  
 \*TR; KRP-297 \*TR; BMS-298585 \*TR; REGAGLITAZAR \*TR; SR-58611 \*TR;  
 TAK-677 \*TR; GP-3034 \*TR; LAF-237 \*TR; P-32-98 \*TR; DPP-728 \*TR;  
 NN-2211 \*TR; TR \*FT  
 [03] ACETOHEXAMIDE \*AE; CHLORPROPAMIDE \*AE; TOLBUTAMIDE \*AE; TOLAZAMIDE  
 \*AE; GLIBENCLAMIDE \*AE; GLIPIZIDE \*AE; GLIMIPERIDE \*AE; REPAGLINIDE  
 \*AE; NATEGLINIDE \*AE; GLIBENCLAMIDE \*AE; MITIGLINIDE \*AE;  
 METFORMIN \*AE; PHENFORMIN \*AE; CIGLITAZONE \*AE; TROGLITAZONE \*AE;  
 ROSIGLITAZONE \*AE; PIOGLITAZONE \*AE; ACARBOSE \*AE; MIGLITOL \*AE;  
 BALAGLITAZONE \*AE; NATOGLITAZONE \*AE; RAGAGLITAZAR \*AE; TESAGLITAZAR  
 \*AE; KRP-297 \*AE; BMS-298585 \*AE; REGAGLITAZAR \*AE; SR-58611 \*AE;  
 TAK-677 \*AE; GP-3034 \*AE; LAF-237 \*AE; P-32-98 \*AE; DPP-728 \*AE;  
 NN-2211 \*AE; AE \*FT

L61 ANSWER 47 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-33933 DRUGU P E Full-text

TITLE: Clinical pharmacokinetics and pharmacodynamics of  
 repaglinide.

AUTHOR: Hatorp V

LOCATION: Hoersholm, Den.

SOURCE: Clin.Pharmacokinet. (41, No. 7, 471-83, 2002) 5 Fig. 4 Tab.  
 48 Ref.

CODEN: CPKNDH ISSN: 0312-5963

AVAIL. OF DOC.: Danish Toxicology Center, Kogle Alle 2, DK-2970 Hoersholm,  
 Denmark. (e-mail: vh@dtc.dk).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Clinical pharmacokinetics and pharmacodynamics of repaglinide (RP) are  
 reviewed. The pharmacokinetics of RP in healthy volunteers, patients with  
 type 2 diabetes, and in special populations (hepatic and renal insufficiency)  
 are analyzed. Drug-drug interactions are presented with reference to protein  
 binding interactions and in-vivo interactions with cimetidine, digoxin,  
 theophylline, warfarin, and rifampicin. Finally, the pharmacodynamics of RP  
 are discussed in relation to dose tolerance, dose response and dosage  
 regimen.

AN 2002-33933 DRUGU P E Full-text

P Pharmacology

E Endocrinology

8 Pharmacokinetics

12 Antidiabetics

66 Drug Interactions

69 Reviews

CT CASES \*FT; HUMAN \*FT; IN-VIVO \*FT; REVIEW \*FT; PHARMACOKINETICS \*FT;  
 PHARMACODYNAMICS \*FT; ANTIDIABETIC \*FT

[01] REPAGLINIDE \*PH; REPAGLINIDE \*DM; AGEE623ZW \*RN; MAIN-TOPIC \*FT;  
 ANTIDIABETICS \*FT; PH \*FT; DM \*FT

RN: 135062-02-1

[02] NATEGLINIDE \*PH; MITIGLINIDE \*PH; KETOCONAZOLE \*DI;

10/519155

RIFAMPICIN \*DI; CIMETIDINE \*DI; DIGOXIN \*DI; THEOPHYLLINE \*DI;  
WARFARIN \*DI; PH \*FT; DI \*FT

L61 ANSWER 48 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-11212 DRUGU P E Full-text

TITLE: Sulfonylurea stimulation of insulin secretion.

AUTHOR: Proks P; Reimann F; Green N; Gribble F; Ashcroft F

CORPORATE SOURCE: Univ.Oxford; Univ.Cambridge

LOCATION: Oxford; Cambridge, U.K.

SOURCE: Diabetes (51, Suppl. 3, S368-S376, 2002) 4 Fig. 1 Tab. 55  
Ref.

CODEN: DIAEAZ ISSN: 0012-1797

AVAIL. OF DOC.: University Laboratory of Physiology, Parks Road, Oxford OX1  
3PT, England. (F.A.). (e-mail: frances.ashcroft@physiol.ox.ac  
.uk).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Sulfonylurea stimulation of insulin secretion is reviewed. The inhibition of KATP channels by imidazolines (phentolamine, cibenzoline), antimalarials (quinine, mefloquine), sulfonylureas (tolbutamide, gliclazide, glimepiride), and benzamido derivatives and the specificity of high-affinity sulfonylurea block are discussed. The location of the sulfonylurea binding site on SUR and interactions between Kir6.1 and SUR are explained. Modulation of sulfonylurea block by PIP2 and modulation of sulfonylurea block by MG nucleotides are considered. Findings indicate that the classification of sulfonylureas, meglitinide derivatives ect can be changed to reflect the functional differences among these drugs, and that they be referred to instead as SUR1-specific and non-SUR1-specific. (conference paper: 3rd Servier - IGIS Symposium, St. Jean Cap Ferrat, France, 2002).

AN 2003-11212 DRUGU P E Full-text

P Pharmacology

E Endocrinology

12 Antidiabetics

69 Reviews

CT REVIEW \*FT; INSULIN \*FT; PANCREAS-HORMONE-METAB. \*FT; ANTIDIABETIC  
\*FT; MODE-OF-ACT. \*FT; IN-VIVO \*FT; LAB.ANIMAL \*FT

[01] MAIN-TOPIC \*FT; ANTIDIABETICS \*FT; PH \*FT

[02] PHENTOLAMINE \*PH; CIBENZOLINE \*PH; QUININE \*PH; MEFLOQUINE \*PH;  
TOLBUTAMIDE \*PH; GLICLAZIDE \*PH; GLIMEPIRIDE \*PH; MEGLITINIDE \*PH;  
MITIGLINIDE \*PH; NATEGLINIDE \*PH; GLIBENCLAMIDE \*PH; GLIPIZIDE  
\*PH; REPAGLINIDE \*PH; PH \*FT

L61 ANSWER 49 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 2001-42236 DRUGU P T E Full-text

TITLE: Insulinotropic maglitinide analogues.

AUTHOR: Dornhorst A

CORPORATE SOURCE: Univ.London

LOCATION: London, U.K.

SOURCE: Lancet (358, No. 9294, 1709-16, 2001) 3 Fig. 78 Ref.

CODEN: LANCAO ISSN: 0140-6736

AVAIL. OF DOC.: Department of Metabolic Medicine, Faculty of Medicine,  
Imperial College, Hammersmith Hospital Campus, Du Cane Road,  
London W12 ONN, England. (e-mail: a.dornhorst@ic.ac.uk).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Insulinotropic maglitinide analogs are reviewed in terms of the pathophysiology of type 2 **diabetes** and the importance of beta cell function, defects in insulin pulsatility and early-phase insulin secretion in those at risk of type 2 **diabetes**. Pharmacological approaches to type 2 **diabetes** are discussed and the mechanism of action, efficacy in clinical trials, combination therapy and pharmacokinetics, safety and tolerability of repaglinide and nateglinide are explored in detail. The ability to preserve beta cell function is compared in nateglinide and glibenclamide. Mitiglinide is also briefly considered along with an evaluation of recent mixed molecules such as BTS-67582. Understanding of the pathophysiology of type 2 **diabetes** is now clearer and this knowledge is beginning to yield new agents of therapeutic promise such as repaglinide and nateglinide.

AN 2001-42236 DRUGU P T E Full-text  
P Pharmacology  
T Therapeutics  
E Endocrinology  
12 Antidiabetics  
64 Clinical Trials  
69 Reviews

CT DIABETES \*TR; CARBOHYDRATE-METAB.DISORDER \*TR; PANCREOPATHY  
\*TR; REVIEW \*FT; IN-VITRO \*FT; IN-VIVO \*FT; CASES \*FT; LAB.ANIMAL \*FT;  
BETA-CELL \*FT; PHARMACOKINETICS \*FT; MODE-OF-ACT. \*FT; INSULIN \*FT;  
CARBOHYDRATE-METAB. \*FT; CLIN.TRIAL \*FT; COMB. \*FT; ANTIDIABETIC \*FT;  
PANCREAS \*FT

[01] MAIN-TOPIC \*FT; ANTIDIABETICS \*FT; TR \*FT; PH \*FT

[02] MEGLITINIDE \*TR; REPAGLINIDE \*TR; METFORMIN \*TR; TROGLITAZONE \*TR;  
NATEGLINIDE \*TR; MITIGLINIDE \*TR; BTS-67582 \*TR; S-21663  
\*PH; S-2166 \*PH; JTT-608 \*PH; MEGLITINIDE \*PH; REPAGLINIDE \*PH;  
METFORMIN \*PH; TROGLITAZONE \*PH; NATEGLINIDE \*PH; MITIGLINIDE  
\*PH; BTS-67582 \*PH; GLIBENCLAMIDE \*PH; TR \*FT; PH \*FT



10/519155

\*\*\*\*\* INVENTOR RESULTS \*\*\*\*\*

=> d his 142

(FILE 'HCAPLUS' ENTERED AT 14:40:20 ON 24 MAY 2007)

L42 6 S L41 NOT L33

=> d que 142

L4 1 SEA FILE=REGISTRY ABB=ON PLU=ON 145375-43-5/RN  
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON 207844-01-7/RN  
L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON MITIGLINIDE/CN  
L8 2 SEA FILE=REGISTRY ABB=ON PLU=ON (L4 OR L5 OR L6)  
L9 97 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR MITIGLINIDE CALCIUM  
HYDRATE/OBI  
L10 87 SEA FILE=HCAPLUS ABB=ON PLU=ON MITIGLINIDE/OBI OR MITI/OBI(W)  
GLINIDE/OBI  
L11 108 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 OR L10  
L13 2160940 SEA FILE=HCAPLUS ABB=ON PLU=ON (INHIBIT?/OBI OR HINDER?/OBI  
OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR  
PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI)  
L19 110617 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABET?/OBI  
L20 54 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND L19  
L22 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 (5A) L20  
L23 QUE ABB=ON PLU=ON AY<2004 OR PRY<2004 OR PY<2004 OR MY  
<2004 OR REVIEW/DT  
L24 17 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L23  
L27 271 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI (3A)  
(POST/OBI(W) PRANDIAL/OBI OR POSTPRANDIAL/OBI)  
L28 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND L27  
L29 13237 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI  
L30 13237 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 OR L29  
L31 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND L30  
L32 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 OR L31  
L33 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 OR L24  
L34 15 SEA FILE=HCAPLUS ABB=ON PLU=ON "MIKOSHIBA IMAO"/AU  
L35 328 SEA FILE=HCAPLUS ABB=ON PLU=ON SUZUKI HISAO/AU  
L36 9 SEA FILE=HCAPLUS ABB=ON PLU=ON KIYONO YUJI/AU  
L37 346 SEA FILE=HCAPLUS ABB=ON PLU=ON (L34 OR L35 OR L36)  
L38 673 SEA FILE=HCAPLUS ABB=ON PLU=ON ("KISSEI PHARMACEUTICAL"/CO  
OR "KISSEI PHARMACEUTICAL"/PA OR "KISSEI PHARMACEUTICAL"/CS OR  
"KISSEI PHARMACEUTICAL CO"/CO OR "KISSEI PHARMACEUTICAL CO  
LTD"/CO OR "KISSEI PHARMACEUTICAL CO LTD"/PA OR "KISSEI  
PHARMACEUTICAL CO LTD"/CS OR "KISSEI PHARMACEUTICAL CO LTD  
CENTRAL RESEARCH LABORATORIES"/CO OR "KISSEI PHARMACEUTICAL CO  
LTD CENTRAL RESEARCH LABORATORIES HOTAKA 399 83 JAPAN"/CS OR  
"KISSEI PHARMACEUTICAL CO LTD JAPAN"/PA OR "KISSEI PHARMACEUTIC  
AL CO LTD JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD NAGANO  
399 8304 JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD PHARMACEUTI  
CAL RESEARCH LABORATORIES"/CO OR "KISSEI PHARMACEUTICAL CO LTD  
PHARMACEUTICAL RESEARCH LABORATORIES NAGANO 399 8304 JAPAN"/CS  
OR "KISSEI PHARMACEUTICAL CO LTD SHINSHU UNIVERSITY"/CO OR  
"KISSEI PHARMACEUTICAL COMPANY"/CO OR "KISSEI PHARMACEUTICAL  
COMPANY LIMITED"/CO OR "KISSEI PHARMACEUTICAL COMPANY LTD"/CO  
OR "KISSEI PHARMACEUTICAL INDUSTRY CO LTD"/CO OR "KISSEI  
PHARMACEUTICAL JAPAN"/PA OR "KISSEI PHARMACEUTICAL JAPAN"/CS)  
L39 722 SEA FILE=HCAPLUS ABB=ON PLU=ON KISSEI PHARMA?/PA,CS,CO  
L40 722 SEA FILE=HCAPLUS ABB=ON PLU=ON L38 OR L39  
L41 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L37 AND L40  
L42 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L41 NOT L33

10/519155

=> d his l60

(FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 14:54:53 ON 24 MAY 2007)

L60 6 S L59 NOT L49

=> d que l60

L4 1 SEA FILE=REGISTRY ABB=ON PLU=ON 145375-43-5/RN  
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON 207844-01-7/RN  
L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON MITIGLINIDE/CN  
L8 2 SEA FILE=REGISTRY ABB=ON PLU=ON (L4 OR L5 OR L6)  
L10 87 SEA FILE=HCAPLUS ABB=ON PLU=ON MITIGLINIDE/OBI OR MITI/OBI(W)  
GLINIDE/OBI  
L13 2160940 SEA FILE=HCAPLUS ABB=ON PLU=ON (INHIBIT?/OBI OR HINDER?/OBI  
OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR  
PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI)  
L19 110617 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABET?/OBI  
L23 QUE ABB=ON PLU=ON AY<2004 OR PRY<2004 OR PY<2004 OR MY  
<2004 OR REVIEW/DT  
L27 271 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI (3A)  
(POST/OBI(W) PRANDIAL/OBI OR POSTPRANDIAL/OBI)  
L29 13237 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI  
L43 84 SEA L8  
L44 172 SEA L10  
L45 10 SEA MITIGLINIDE CALCIUM HYDRATE  
L46 173 SEA (L43 OR L44 OR L45)  
L47 110 SEA L46 AND (L19 OR L27 OR L29)  
L48 46 SEA L47 AND L23  
L49 33 SEA L48 (P) L13  
L50 27 SEA MIKOSHIBA I?/AU  
L52 34 SEA SUZUKI HISAO/AU  
L53 2 SEA KIYONO YUJI/AU  
L54 63 SEA L50 OR L52 OR L53  
L55 2 SEA L50 AND L52 OR L53  
L56 2 SEA L54 AND L46  
L57 2 SEA L55 OR L56  
L58 6 SEA L54 AND (L19 OR L27 OR L29)  
L59 6 SEA L57 OR L58  
L60 6 SEA L59 NOT L49

=> dup rem l42 l60

PROCESSING COMPLETED FOR L42

PROCESSING COMPLETED FOR L60

L62 10 DUP REM L42 L60 (2 DUPLICATES REMOVED)  
ANSWERS '1-6' FROM FILE HCAPLUS  
ANSWER '7' FROM FILE MEDLINE  
ANSWER '8' FROM FILE BIOSIS  
ANSWER '9' FROM FILE EMBASE  
ANSWER '10' FROM FILE DRUGU

=> d l62 1-6 ibib abs

L62 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1  
ACCESSION NUMBER: 2004:836630 HCAPLUS Full-text  
DOCUMENT NUMBER: 142:384723  
TITLE: Pharmacological and clinical profile of mitiglinide  
calcium hydrate (Glufast), a new insulinotropic agent  
with rapid onset  
AUTHOR(S): Ojima, Kazuma; Kiyono, Yuji; Kojima, Masami

10/519155

CORPORATE SOURCE: Pharmacol. Res. Lab. R & D, Kissei Pharm. Co.,  
Ltd., Nagano, 399-8304, Japan  
SOURCE: Nippon Yakurigaku Zasshi (2004), 124(4), 245-255  
CODEN: NYKZAU; ISSN: 0015-5691  
PUBLISHER: Nippon Yakuri Gakkai  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese

AB A review. Mitiglinide calcium hydrate (mitiglinide, Glufast) is a new insulinotropic agent of the glinide class with rapid onset. Mitiglinide is thought to stimulate insulin secretion by closing the ATP-sensitive K<sup>+</sup> (KATP) channels in pancreatic  $\beta$ -cells, and its early insulin release and short duration of action would be effective in improving postprandial hyperglycemia. In studies of various cloned KATP channels, mitiglinide shows a higher selectivity for the  $\beta$ -cell type of SUR1/Kir6.2 than the cardiac and smooth muscle types of KATP channels in comparison with glibenclamide and glimepiride. In vitro and in vivo studies demonstrated the insulinotropic effect of mitiglinide is more potent than that of nateglinide, and mitiglinide surpassed in controlling postprandial hyperglycemia in normal and diabetic animals. In clin. trials, treatment with mitiglinide provided lasting improvement of postprandial hyperglycemia in Type 2 diabetic patients and decreased the fasting plasma glucose levels and HbA1C values. The incidence of adverse events related to mitiglinide were nearly equivalent to placebo; in particular there was no difference with the frequency of hypoglycemia. The results from these studies indicated that mitiglinide could be expected to possess good therapeutic features of being effective in reducing postprandial glucose excursions in the early stage of Type 2 diabetes and less incidence of events suggestive of hypoglycemia.

L62 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:404898 HCAPLUS Full-text  
DOCUMENT NUMBER: 146:372816  
TITLE: Mitiglinide and  $\alpha$ -glucosidase inhibitor  
combination for type 2 diabetes therapy  
INVENTOR(S): Kiyono, Yuji; Okubo, Yoshio; Mototani,  
Katsumi; Mikoshiba, Imao  
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 11pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
JP 2007091641	A	20070412	JP 2005-283608	20050929
PRIORITY APPLN. INFO.:			JP 2005-283608	20050929

AB Disclosed are a pharmaceutical preparation for controlling the condition of type 2 diabetes comprising the combination of mitiglinide or a pharmacol. acceptable salt or hydrate thereof and an  $\alpha$ -glycosidase inhibitor, e.g., voglibose. The pharmaceutical preparation shows a potent effect of decreasing the morning fasting blood glucose level, the postprandial blood glucose level and HbA1c in a patient with type 2 diabetes and can ameliorate insulin resistance.

L62 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2006:1157536 HCAPLUS Full-text

10/519155

DOCUMENT NUMBER: 145:477898  
 TITLE: Combined pharmaceutical preparation for treatment of type 2 diabetes  
 INVENTOR(S): Kiyono, Yuji; Okubo, Yoshio; Hontani, Katsumi; Mikoshiba, Imao; Ojima, Kazuma  
 PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 29pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006115115	A1	20061102	WO 2006-JP308110	20060418
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: JP 2005-121862 A 20050420  
 JP 2005-166314 A 20050607

AB Disclosed are a pharmaceutical preparation for controlling the condition of type 2 diabetes, the pharmaceutical preparation comprising the combination of mitiglinide or a pharmacol. acceptable salt or hydrate thereof and an  $\alpha$ -glycosidase inhibitor (e.g., voglibose, acarbose); and a therapeutic method using the pharmaceutical preparation. The pharmaceutical preparation shows an extremely potent effect of decreasing the morning fasting blood glucose level, the postprandial blood glucose level and HbA1c in a patient with type 2 diabetes and can ameliorate glucose spike, insulin resistance and lipid metabolism.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L62 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:83073 HCAPLUS Full-text

DOCUMENT NUMBER: 124:165270

TITLE: Therapeutics for peripheral circulation disorders containing (pyridylmethyl)pyrrolidine derivative

INVENTOR(S): Mikoshiba, Imao; Myata, Hiroshi; Komatsu, Hidetada; Hoyano, Takeshi; Kiguchi, Sumyoshi

PATENT ASSIGNEE(S): Kissei Pharmaceutical, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

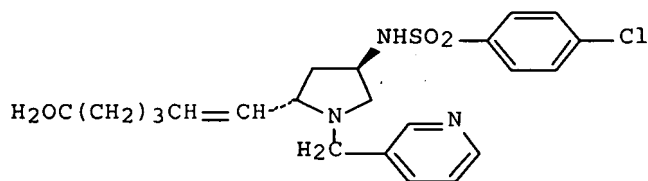
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07304671	A	19951121	JP 1994-130781	19940509

PRIORITY APPLN. INFO.:  
GI

JP 1994-130781

19940509



AB Therapeutics for symptoms caused by peripheral circulation disorders contain the title derivative (I) or its pharmacol. acceptable salts. The therapeutics are useful for treatment of rhigosis (cool sensation), numbness, and pain. I.HCl (preparation given) significantly improved neurotransmission rate in rats with streptozotocin-induced peripheral circulation disorder.

L62 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:115295 HCAPLUS Full-text

DOCUMENT NUMBER: 88:115295

TITLE: Effect of a combined preparation of aluminum dihydroxyallantoinate and meta-magnesium aluminosilicate (Alanta) on acute gastritis in beagles

AUTHOR(S): Azuma, Hiroshi; Shibata, Nobuo; Mikoshiba, Imao; Minamide, Seiki; Naito, Jun; Matsuda, Kuniaki; Kumazawa, Nariyuki

CORPORATE SOURCE: Div. Pharmacol., Kissei Pharm. Co., Ltd., Matsumoto City, Japan

SOURCE: Oyo Yakuri (1977), 13(3), 389-98  
CODEN: OYYAA2; ISSN: 0369-8033

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB The inhibitory effect of Alanta [65775-48-6] on gastritis was demonstrated by histol. examination and also by determination of fibrinolysis.

L62 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:99164 HCAPLUS Full-text

DOCUMENT NUMBER: 88:99164

TITLE: Pharmacological analysis of the combined effect of aluminum dihydroxyallantoinate and meta-magnesium aluminosilicate

AUTHOR(S): Azuma, Hiroshi; Naito, Jun; Tamaoki, Hiroshi; Amaki, Masaharu; Mikoshiba, Imao; Akahane, Masuo

CORPORATE SOURCE: Div. Pharmacol., Kissei Pharm. Co. Ltd., Matsumoto City, Japan

SOURCE: Oyo Yakuri (1977), 13(3), 383-7  
CODEN: OYYAA2; ISSN: 0369-8033

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB Aldioxa [5579-81-7] (Al dihydroxyallantoinate) dose-dependently inhibited stress-induced ulcer in rats. The ED50 of the drug was 523 mg/kg. A slight

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inhibition of the stress-induced ulcer was elicited by treatment with metamagnesium aluminosilicate (MAS) [1327-43-1]. The ED50 of MAS was 25,500 mg/kg. When aldioxa and MAS were administered in combination in the ratio of 1/9, 1/19 and 1/29, the ED50 values were 1194, 1819 and 5725 mg/kg, resp. The inhibitory effect on the water immersion stress-induced ulcer was also potentiated by combined treatment with aldioxa and MAS. Aldioxa and MAS inhibited pylorus-ligation-induced ulcer in a dose-dependent manner. The ED50 values were 446 and 406 mg/kg, resp. When aldioxa and MAS were administered in the ratio of 1/9, 1/1 and 2/1, the ED50 values were 369, 395, and 405 mg/kg, resp. The inhibitory effect on pylorus-ligation ulcer induction was enhanced in an additive manner by the combined treatment.

=> d 162 7-10 ibib ab

L62 ANSWER 7 OF 10 MEDLINE on STN  
ACCESSION NUMBER: 2003177108 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 12694990  
TITLE: Rationale and evidence for the use of oxcarbazepine in neuropathic pain.  
AUTHOR: Carrazana Enrique; Mikoshiba Imao  
CORPORATE SOURCE: Neuroscience, Clinical Development and Medical Affairs, Novartis Pharmaceuticals, East Hanover, NJ 07936-1080, USA.  
SOURCE: Journal of pain and symptom management, (2003 May) Vol. 25, No. 5 Suppl, pp. S31-5. Ref: 25  
Journal code: 8605836. ISSN: 0885-3924.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200307  
ENTRY DATE: Entered STN: 17 Apr 2003  
Last Updated on STN: 3 Jul 2003  
Entered Medline: 2 Jul 2003

AB Oxcarbazepine is a second-generation antiepileptic drug (AED) with proven efficacy in managing partial epileptic seizures, with or without secondary generalization, in adults and children. The overlap between the underlying pathophysiologic mechanisms of some epilepsy models and neuropathic pain models supports the rationale for using certain AEDs in the treatment of neuropathic pain. Several AEDs have reportedly produced analgesia in a range of neuropathic pains, including painful diabetic neuropathy (PDN) and post-herpetic neuralgia. Increasing evidence suggests that oxcarbazepine can provide significant analgesia in several neuropathic pain conditions, including trigeminal neuralgia and PDN, and is also may be effective in treating neuropathic pain refractory to other AEDs, such as carbamazepine and gabapentin. The analgesic effects of oxcarbazepine, and its generally improved safety and tolerability profile compared with other standard AEDs, suggests that oxcarbazepine will be an important addition to the neuropathic pain armamentarium. The rationale and evidence to support the efficacy of oxcarbazepine are presented here.

L62 ANSWER 8 OF 10 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN  
ACCESSION NUMBER: 2000:442810 BIOSIS Full-text  
DOCUMENT NUMBER: PREV200000442810  
TITLE: Re-evaluation of exercise prescription for Japanese type 2 diabetic patients by ventilatory threshold.

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AUTHOR(S): Kunitomi, Mie [Reprint author]; Takahashi, Kayo; Wada, Jun;  
Suzuki, Hisao; Miyatake, Nobuyuki; Ogawa, Saeko;  
Ohta, Sachiko; Sugimoto, Hikaru; Shikata, Kenichi; Makino,  
Hirofumi  
CORPORATE SOURCE: Department of Medicine III, Okayama University Medical  
School, 2-5-1 Shikata-cho, Okayama, 700-8558, Japan  
SOURCE: Diabetes Research and Clinical Practice, (October, 2000)  
Vol. 50, No. 2, pp. 109-115. print.  
CODEN: DRCPE9. ISSN: 0168-8227.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 18 Oct 2000  
Last Updated on STN: 10 Jan 2002

AB Prescription of aerobic exercise for Type 2 diabetes mellitus (Type 2 DM) in clinical practice is frequently based on exercise intensity at maximum heart rate ( $60 < \text{HRmax} < 79\%$ ), heart rate reserve ( $50 < \text{HRreserve} < 74\%$ ), and rating of perceived exertion ( $12 < \text{RPE} < 13$ ). We examined these parameters in Japanese males with Type 2 DM at ventilatory threshold (VT) to investigate the exercise capacity of Type 2 DM patients and re-evaluate the exercise prescription. Fifty-six Japanese Type 2 DM males without autonomic neuropathy (age,  $53.5 \pm 7.7$  years; body mass index (BMI),  $23.7 \pm 3.6$  kg/m<sup>2</sup>) were enrolled and compared with 56 age- and BMI-matched healthy Japanese males. VT was determined breath by breath during exercise test using a ramp protocol and rates of oxygen consumption (VO<sub>2</sub>), work rate (WR), HR, DELTAHR, %HRmax, %HRreserve, and RPE were measured at VT. Type 2 DM patients had significantly lower VO<sub>2</sub> ( $3.6 \pm 0.4$  metabolic equivalents (METs)) and WR ( $62 \pm 14$  W) than controls (VO<sub>2</sub>,  $3.9 \pm 0.6$  METs; WR,  $74 \pm 13$  W). %HRreserve, ( $32.6 \pm 7.7\%$ ) was also significantly lower compared with controls ( $37.6 \pm 8.3\%$ ), while %HRmax, was not different. RPE was also similar in diabetics ( $12.4 \pm 1.5$ ) and controls ( $12.9 \pm 1.2$ ), however, it was significantly lower in diabetic patients aged 60-69 years ( $11.8 \pm 2.0$ ) and those with distal symmetric sensory neuropathy ( $12.2 \pm 1.0$ ). Our results indicate reduced exercise capacity in Japanese Type 2 DM males and the exercise intensity of  $60\% \text{HRmax}$ ,  $30\% \text{HRreserve}$ , and RPE 12 is recommended in elderly diabetics and those with diabetic sensory neuropathy.

L62 ANSWER 9 OF 10 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003151062 EMBASE Full-text  
TITLE: Rationale and evidence for the use of oxcarbazepine in neuropathic pain.  
AUTHOR: Carrazana E.; Mikoshiba I.  
CORPORATE SOURCE: Dr. E. Carrazana, Neurosci., Clin. Devmt./Med. Affairs,  
Novartis Pharmaceuticals, Building 403, 59 Route 10, East  
Hanover, NJ 07936-1080, United States  
SOURCE: Journal of Pain and Symptom Management, (1 May 2003) Vol.  
25, No. 5 SUPPL., pp. S31-S35. .  
Refs: 25  
ISSN: 0885-3924 CODEN: JPSMEU  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 003 Endocrinology  
008 Neurology and Neurosurgery  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 24 Apr 2003  
Last Updated on STN: 24 Apr 2003

AB Oxcarbazepine is a second-generation antiepileptic drug (AED) with proven efficacy in managing partial epileptic seizures, with or without secondary generalization, in adults and children. The overlap between the underlying pathophysiologic mechanisms of some epilepsy models and neuropathic pain models supports the rationale for using certain AEDs in the treatment of neuropathic pain. Several AEDs have reportedly produced analgesia in a range of neuropathic pains, including painful diabetic neuropathy (PDN) and post-herpetic neuralgia. Increasing evidence suggests that oxcarbazepine can provide significant analgesia in several neuropathic pain conditions, including trigeminal neuralgia and PDN, and is also may be effective in treating neuropathic pain refractory to other AEDs, such as carbamazepine and gabapentin. The analgesic effects of oxcarbazepine, and its generally improved safety and tolerability profile compared with other standard AEDs, suggests that oxcarbazepine will be an important addition to the neuropathic pain armamentarium. The rationale and evidence to support the efficacy of oxcarbazepine are presented here. .COPYRG. 2003 U.S. Cancer Pain Relief Committee. Published by Elsevier. All rights reserved.

L62 ANSWER 10 OF 10 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2003-26991 DRUGU T S Full-text  
 TITLE: Neuropathic pain: from mechanisms to treatment strategies.  
 Rationale and evidence for the use of oxcarbazepine in  
 neuropathic pain.  
 AUTHOR: Carrazana E; Mikoshiba I  
 CORPORATE SOURCE: Novartis; Kissei  
 LOCATION: East Hanover, N.J., USA; Tokyo, Jap.  
 SOURCE: J.Pain Symptom Manage. (25, No. 5, Suppl., S31-S35, 2003) 1  
 Fig. 1 Tab. 25 Ref.  
 CODEN: JPSMEU ISSN: 0885-3924  
 AVAIL. OF DOC.: Neuroscience, Clinical Development and Medical Affairs,  
 Novartis Pharmaceuticals, Building 403, Room 362, 59 Route  
 10, East Hanover, NJ, 07936-1080, U.S.A.  
 LANGUAGE: English  
 DOCUMENT TYPE: Journal  
 FIELD AVAIL.: AB; LA; CT  
 FILE SEGMENT: Literature

AB The use of oxcarbazepine in neuropathic pain is reviewed. Oxcarbazepine as a treatment for neuropathic pain including clinical evidence in trigeminal neuralgia, other neuropathic pain conditions and painful diabetic neuropathy are discussed. Oxcarbazepine is an effective and well tolerated treatment for neuropathic pain. This efficacy has been noted in a broad range of neuropathic pain conditions, including trigeminal neuralgia and painful diabetic neuropathy, and in patients refractory to other antiepileptic drugs, such as carbamazepine and gabapentin.



=> d his nofile

(FILE 'HOME' ENTERED AT 14:30:01 ON 24 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 14:31:22 ON 24 MAY 2007

L1 1 SEA ABB=ON PLU=ON US20050215607/PN  
D ALL  
L2 1 SEA ABB=ON PLU=ON US20050267195/PN  
D ALL  
L3 2 SEA ABB=ON PLU=ON L1 OR L2

FILE 'REGISTRY' ENTERED AT 14:34:02 ON 24 MAY 2007

L4 1 SEA ABB=ON PLU=ON 145375-43-5/RN  
L5 1 SEA ABB=ON PLU=ON 207844-01-7/RN  
L6 1 SEA ABB=ON PLU=ON MITIGLINIDE/CN  
L7 0 SEA ABB=ON PLU=ON MITIGLINIDE CALCIUM HYDRATE/CN  
L8 2 SEA ABB=ON PLU=ON (L4 OR L5 OR L6)

FILE 'HCAPLUS' ENTERED AT 14:35:34 ON 24 MAY 2007

L9 97 SEA ABB=ON PLU=ON L8 OR MITIGLINIDE CALCIUM HYDRATE/OBI  
L10 87 SEA ABB=ON PLU=ON MITIGLINIDE/OBI OR MITI/OBI (W) GLINIDE/OBI  
L11 108 SEA ABB=ON PLU=ON L9 OR L10  
L12 3944 SEA ABB=ON PLU=ON DIABET?/OBI (L) (PROGRESS?/OBI OR COMPLICAT  
?/OBI)  
L13 2160940 SEA ABB=ON PLU=ON (INHIBIT?/OBI OR HINDER?/OBI OR IMPED?/OBI  
OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR PREVENT?/OBI OR  
BLOCK?/OBI OR ELIMINAT?/OBI)  
L14 1486 SEA ABB=ON PLU=ON L12 AND L13  
L15 1486 SEA ABB=ON PLU=ON L12 (P) L13  
L16 3 SEA ABB=ON PLU=ON L10 AND L15  
D SCAN

FILE 'STNGUIDE' ENTERED AT 14:39:04 ON 24 MAY 2007

FILE 'HCAPLUS' ENTERED AT 14:40:20 ON 24 MAY 2007

L17 3 SEA ABB=ON PLU=ON L11 (P) L12  
L18 0 SEA ABB=ON PLU=ON L17 NOT L16  
E DIABETS+PFT, OLD, NT/CT  
L19 110617 SEA ABB=ON PLU=ON DIABET?/OBI  
L20 54 SEA ABB=ON PLU=ON L11 AND L19  
L21 28 SEA ABB=ON PLU=ON L13 AND L20  
L22 28 SEA ABB=ON PLU=ON L13 (5A) L20  
D KWIC 1-5  
D L22 TI 1-5  
L23 QUE ABB=ON PLU=ON AY<2004 OR PRY<2004 OR PY<2004 OR MY<2004  
OR REVIEW/DT  
L24 17 SEA ABB=ON PLU=ON L22 AND L23  
L25 3 SEA ABB=ON PLU=ON L10 AND L12  
L26 17 SEA ABB=ON PLU=ON L24 OR L25  
L27 271 SEA ABB=ON PLU=ON HYPERGLYCEM?/OBI (3A) (POST/OBI (W) PRANDIAL/  
OBI OR POSTPRANDIAL/OBI)  
L28 3 SEA ABB=ON PLU=ON L11 AND L27  
D TI 1-3  
L29 13237 SEA ABB=ON PLU=ON HYPERGLYCEM?/OBI  
L30 13237 SEA ABB=ON PLU=ON L27 OR L29  
L31 7 SEA ABB=ON PLU=ON L11 AND L30  
L32 7 SEA ABB=ON PLU=ON L28 OR L31  
L33 24 SEA ABB=ON PLU=ON L32 OR L24

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SAVE TEMP L33 FIN155HCAP/A
E MIKOSHIBA I?/AU
L34      15 SEA ABB=ON  PLU=ON  "MIKOSHIBA IMAO"/AU
E SUZUKI H?/AU
L35      328 SEA ABB=ON  PLU=ON  SUZUKI HISAO/AU
E KIYONO Y?/AU
L36      9 SEA ABB=ON  PLU=ON  KIYONO YUJI/AU
L37      346 SEA ABB=ON  PLU=ON  (L34 OR L35 OR L36)
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L38      673 SEA ABB=ON  PLU=ON  ("KISSEI PHARMACEUTICAL"/CO OR "KISSEI
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LTD"/CS OR "KISSEI PHARMACEUTICAL CO LTD CENTRAL RESEARCH
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OR "KISSEI PHARMACEUTICAL INDUSTRY CO LTD"/CO OR "KISSEI
PHARMACEUTICAL JAPAN"/PA OR "KISSEI PHARMACEUTICAL JAPAN"/CS)
L39      722 SEA ABB=ON  PLU=ON  KISSEI PHARMA?/PA,CS,CO
L40      722 SEA ABB=ON  PLU=ON  L38 OR L39
L41      8 SEA ABB=ON  PLU=ON  L37 AND L40
L42      6 SEA ABB=ON  PLU=ON  L41 NOT L33
SAVE TEMP L42 FIN155HCAAU/A
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FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 14:54:53 ON 24 MAY 2007

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L43      84 SEA ABB=ON  PLU=ON  L8
L44      172 SEA ABB=ON  PLU=ON  L10
L45      10 SEA ABB=ON  PLU=ON  MITIGLINIDE CALCIUM HYDRATE
L46      173 SEA ABB=ON  PLU=ON  (L43 OR L44 OR L45)
L47      110 SEA ABB=ON  PLU=ON  L46 AND (L19 OR L27 OR L29)
L48      46 SEA ABB=ON  PLU=ON  L47 AND L23
L49      33 SEA ABB=ON  PLU=ON  L48 (P) L13
D TRIAL 1-5
SAVE TEMP L49 FIN155MULTI/A
L50      27 SEA ABB=ON  PLU=ON  MIKOSHIBA I?/AU
L51      22092 SEA ABB=ON  PLU=ON  SUZUKI H?/AU
L52      34 SEA ABB=ON  PLU=ON  SUZUKI HISAO/AU
L53      2 SEA ABB=ON  PLU=ON  KIYONO YUJI/AU
L54      63 SEA ABB=ON  PLU=ON  L50 OR L52 OR L53
L55      2 SEA ABB=ON  PLU=ON  L50 AND L52 OR L53
L56      2 SEA ABB=ON  PLU=ON  L54 AND L46
L57      2 SEA ABB=ON  PLU=ON  L55 OR L56
L58      6 SEA ABB=ON  PLU=ON  L54 AND (L19 OR L27 OR L29)
L59      6 SEA ABB=ON  PLU=ON  L57 OR L58
D L59 TI 1-6
L60      6 SEA ABB=ON  PLU=ON  L59 NOT L49
SAVE TEMP L60 FIN155MULAU/A
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FILE 'STNGUIDE' ENTERED AT 15:06:18 ON 24 MAY 2007

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D QUE L33
D QUE L49
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10/519155

FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 15:07:58 ON 24  
MAY 2007

L61           49 DUP REM L33 L49 (8 DUPLICATES REMOVED)  
              ANSWERS '1-24' FROM FILE HCAPLUS  
              ANSWERS '25-42' FROM FILE MEDLINE  
              ANSWERS '43-45' FROM FILE EMBASE  
              ANSWERS '46-49' FROM FILE DRUGU  
              D L61 1-24 IBIB ED ABS HITIND  
              D L61 25-49 IBIB AB IND  
              D QUE L42  
              D QUE L60  
L62           10 DUP REM L42 L60 (2 DUPLICATES REMOVED)  
              ANSWERS '1-6' FROM FILE HCAPLUS  
              ANSWER '7' FROM FILE MEDLINE  
              ANSWER '8' FROM FILE BIOSIS  
              ANSWER '9' FROM FILE EMBASE  
              ANSWER '10' FROM FILE DRUGU  
              D L62 1-6 IBIB ABS  
              D L62 7-10 IBIB AB



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#1	Search mitiglinide and (diabetic OR diabetes or postprandial or glycemic or glycemia or complications)	17:34:52	<u>33</u>
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